THURSDAY 7:30-8:45 AM—JUNE 18, 1964

REFRESHER COURSES

A-1* *Thyroid Function Studies*—WILLIAM H. BEIERWALTES. (Study A)

The theory of the thyroidal I^{131} uptake test is reviewed. The 1-4 hour tests are good diagnostic tests for the diagnosis of Grave's disease but the 24 hour test is best in detecting hypothyroidism. The 6 hour test is the most convenient compromise. The 2, 4, 6 and 24 hour tests together give data on I^{131} transit time. The PBI^{131} tells more about transit time than hyper- or hypothyroidism. The I^{131} uptake is at its worst in nodular goiters. The T-3 RBC (or resin) uptake tests are helpful when other tests fail. Thyroid scanning describes the morphological genesis of colloid nodular goiter and locates functioning metastases. Point counting used with scans helps quantitate uptake in metastases.

A-2 *Radiation Safety*—ROSALYN S. YALOW. (Study B)

To ensure that the medical usage of ionizing radiations be consistent with maximum safety for patient, staff and community certain basic precautions must be observed. These precautions have been formulated into specific legal regulations and quasi-legal recommendations of national and international advisory groups. In this presentation the following topics will be discussed: (1) biological effects of radiation at medical usage levels; (2) principles of radiation safety in radioisotope installation; (3) recommendations of NCRP, ICRP and relevant NBS handbooks; (4) problems of monitoring and waste disposal; (5) application of common sense to the management of radiation safety in practical laboratory and medical situations.

A-3 *Radioisotope Physics*—ROBERT H. ROHRER. (Study C)

The course shall include a review of current understanding of the physical constitution, the activation, and the molecular behavior of radioisotopes followed by an introduction of an acceptable picture of radioactive decay processes, the elementary nature of atomic radiations, and the mechanisms by which these radiations contribute to radiobiological doses. These fundamentals shall be related to tracer level detection and measurement, to scanning, to internal dose estimates, and to other general problems encountered in the practice of nuclear medicine.

A-4 *Problems of Scanning*—C. C. HARRIS. (Study D)

Scanning, like other diagnostic studies, consists of a closed-loop information flow. *Physician*—makes decision that scan would be useful (this may require choice of tracer material)—administers tracer to patient. *Patient*—metabolizes, transports, concentrates or otherwise distributes tracer material—tracer emits gamma rays. *Detector-Spectrometer System*—"counts" gamma rays—selects them as to "kind" and origin—presents information for recording. *Data Recording*—puts "counted" information in forms that may be interpreted. *Physician*—interprets and uses information for benefit of patient, closing the loop. The problems in scanning are the distortions, of the necessarily scarce information, that occur at any part of the cycle.

A-5 *Effects of Radioiactivity Upon The Mammalian Organism*—MIRIAM P. FINKEL. (Study E)

The course will be concerned with the pathologic consequences of the exposure of experimental animals to radionuclides (1) when the chemical form of the nuclide and the route of administration vary; (2) when different kinds of animals are used; (3) when different total amounts of activity are given; (4) when nuclides with different physical characteristics are used; and (5) when the pattern of exposure is changed. Particular attention will be given to decrease in life span and increase in cancer.

**Serial numbers (A-1, F-3, S-5, etc) refer to program identification and abstracts, which are printed in the Abstract Book and in the May 1964 issue of THE JOURNAL OF NUCLEAR MEDICINE.*

THURSDAY MORNING—JUNE 18, 1964
DIAGNOSTIC SESSIONS—SCANNING

Chairman, THOMAS CARLILE

EMPIRE ROOM

T-1 *"Detection Of Occult Bone Metastases By Photoscanning with Radiostrontium."* DAVID M. SKLAROFF, N. DAVID CHARKES, and J. GERSHON-COHEN, (Dept. of Radiology, Albert Einstein Medical Center, Northern Division, Philadelphia, Pennsylvania)

Conventional roentgenography of bone, particularly of vertebrae, frequently fails to visualize metastatic foci. Bone adjacent to tumor responds by increased osteoblastic activity which can be detected by photoscanning with strontium-85 or -87m.

One hundred eighteen cancer patients with known or suspected metastases were scanned with Sr^{85}. In 26, the scan showed abnormally increased localized strontium deposition despite negative roentgenograms, and in the absence of symptoms in some patients. Only 4 false negative scans were found. In the other patients, scan findings correlated closely with roentgenograms. Bone biopsies confirmed Sr^{85} localization in 17 patients, 4 of whom had negative roentgenograms.

Sr^{87m} showed localization similar to Sr^{85} in 17 patients. Its short halflife (2.8 hours) permits repetitive evaluations following roentgen or hormonal therapy, and doses up to 1.5 mc considerably shorten scanning time.

Photoscanning of bone with Sr^{85} and ^{87m} has proven to be more sensitive than conventional roentgenography for detection of occult metastases, and is of considerable value to the radiation therapist in planning treatment portals.

T-2 *"Chlormerodrin Scintiecephaloscanning For the Detection And Localization of Non-neoplastic Intracranial Disease."* ROBERT T. MORRISON, ADEL K. AFIFI, MAURICE W. VAN ALLEN, and TITUS C. EVANS (College of Medicine, State University of Iowa, Iowa City, Iowa.)

The primary application of brain scanning has been for the detection and localization of brain tumors. Little has been written concerning its application to non-neoplastic intracranial disease. Mercury-203 chlormerodrin brain scans were performed on 600 patients suffering from a variety of disorders of the brain. Sixteen of 38 patients with a diagnosis of cerebral infarction had abnormal scintiscans which localized correctly the lesion to that part of the brain which was suspected to be involved clinically. Subsequent scintiscans on 4 of these patients 5 to 10 months later yielded normal scintiscans. Twenty-two patients with a clinical diagnosis of atherosclerotic cerebrovascular disease had normal scintiscans. The lesion was localized correctly in 5 patients who had intracerebral hematomas. Three of 5 patients with arteriovenous malformations and 2 of 5 with subdural hematomas had abnormal scans. It is apparent that many lesions other than brain tumors show abnormalities with this procedure.

T-3 *"The Diagnosis Of Pulmonary Embolism By Radioisotope Scanning."* HENRY N. WAGNER, JR., DAVID C. SABISTON, and MASAHIRO IIO, (Departments of Medicine, Radiology and Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland.)

Massive pulmonary embolism remains and important cause of death. The surgical approach to this disease has been impeded by uncertainty of diagnosis in many cases. In 44 dogs with experimental pulmonary emboli and 70 patients with pulmonary diseases, including massive embolism, a method was developed which has been found to be a safe, rapid and effective means of determining the site and extent of pulmonary embolism.

Human serum albumin labeled with I^{131} or Cr^{51} was aggregated into particles 10 to 50 micra in diameter. When injected intravenously, these particles lodge in the pulmonary arterioles and capillaries. The distribution of radioactivity can be clearly delineated by scintillation scanning and is directly proportional to regional pulmonary blood flow. The method has proven safe from the standpoint of hemodynamic effect, radiation hazard and antigenicity.

An experimental technic was developed which permitted removal of large emboli after varying periods of time. In all animals the embolus was correctly localized by scanning. Following removal of the embolus, *in situ* thrombosis was regularly found distal to the point of obstruction. Restoration of pulmonary circulation was determined by serial scanning and found to be a function of the duration of occlusion of the involved vessel. Clinically, the method has been of great value in the immediate diagnosis and accurate localization of pulmonary embolism.

T-4 *"Topographic Distribution Of Amoebic Abscess Studied By Liver Scanning."* A. CUARON, B. SEPULVEDA, and L. LANDA, (Servicio de Gastroenterología and Servicio de Radioisótopos, Hospital General, Centro Médico Nacional; Comisión Nacional de Energía Nuclear, Mexico).

One hundred six amoebic abscesses of the liver were studied by liver scanning in two directions, antero-posterior and right lateral, after the administration of I^{131}-Rose Bengal. 83 per cent of the abscesses were localized at the right hepatic lobes and only 17 per cent at the left lobe. The more affected regions of the right lobe were: the posterior surface (54.7 per cent), the external surface (50.9 per cent) and the upper surface (34.9 per cent). The more common localizations in these regions were: the upper third of the posterior surface (28.3 per cent), the two external thirds of the upper surface (23.0 per cent) and the lower third of the external surface (21.7 per cent).

The results were analyzed in order to find out which direction is the best for each localization. The antero-posterior direction alone, located 85.8 per cent of the abscesses; the right lateral direction demonstrated only the 77.3 per cent. The two directions together demonstrated the 99.0 per cent of the abscesses. The antero-posterior was the best position for the localization of the abscesses located at the left lobe and at the upper two thirds of the external surface of the right lobe, between the anterior and posterior surfaces and at the central part of the lower third of the anterior surface. The lateral position was the best for the localization of the abscesses located at the central third of the posterior surface and at the lower third of the central region of the right lobe. In other regions both directions had the same value. Only one abscess was not demonstrated at the first attempt with this procedure. It was localized a few days later on a second scanning at the external upper third of the posterior surface. The importance of this method for the localization of amoebic abscesses before surgery and medical treatment and for the control of the evolution of the disease is discussed.

T-5 *"A New Organ Scan Display In Polaroid Color."* RALPH ADAMS and HENRY L. JAFFE, (Cedars of Lebanon Hospital, Los Angeles, California.)

A new accessory instrument was developed for the production of "photoscans" in Polaroid color. The instrument consists of a modified cathode ray oscilloscope, camera, a strip of color filters, servomechanism, and associated electronic circuits.

The position of the electron beam on the screen is made to track with the mechanical position of the scan detector by means of ganged helical potential dividers driven by the scan mechanism and connected to DC power supplies. The electron beam is normally "off" and is keyed "on" by a square wave generator triggered by the output of the analyzer of the scanner. A saw tooth signal is superimposed on the vertical deflection plates to produce a vertical sweep to coincide with spacing between scan lines. Finally, magnification control is achieved by connection to deflection plates through four-gang potential dividers.

The filter strip, between the screen and camera lens, is driven from color to color by the servomechanism operated from the ratemeter circuit of the scanner, so that full scale readings record in red, background in purple, and other rates in intermediate spectral colors during a time exposure.

The instrument may be operated simultaneously with conventional "photoscan" and stylus recording. It is calibrated to provide quantitiative information from the color coding. Furthermore, color contrast is achieved without loss of latitude.

A comparison will be presented between the color scanning print-out system developed by Gerald J. Hine, and our color photoscans made in Polaroid color.

T-6 *"Abnormalities Of Distribution of Marrow Shown With Fe^{52} And The Positron Scintillation Camera."* DONALD VAN DYKE, and HAL ANGER (Donner Laboratory, University of California, Berkeley, California.)

Development of the positron camera has made it possible to obtain detailed visualization of the marrow compartment in the living subject. The first studies done using this technique have demonstrated remarkable differences in marrow distribution associated with various disease states. Demonstration of gross changes in distribution of marrow within the skeleton has been possible in the past using Fe^{59} and various scanning devices, but the positron camera and Fe^{52} provide detail previously available only by laborious post-mortem examination.

For best visualization of the marrow, scintiphotos were taken when the blood level was low and marrow uptake was high, about 15 hours after intravenous administration of Fe^{52}. Satisfactory pictures were obtained in adults with 10 minutes exposure after as little as 50-100 microcurie administered dose.

Visualization of the marrow in normal adults has shown the same distribution found in past clinical-pathological studies, marrow throughout the pelvis, spine, sternum and ribs with some in the proximal ends of the extremities. Markedly abnormal distribution of marrow has been demonstrated both in primary blood diseases and in one case of primary bone disease (Paget's disease). Extension of the marrow into the extremities has been demonstrated in primary polycythemia and following chronic blood loss, whereas the distribution of marrow was essentially normal in cases of polycythemia secondary to hypoxia (congenital heart disease). In one case of Paget's disease increased amounts of marrow were found in the parts of the skeleton most affected by the disease.

THURSDAY MORNING—JUNE 18, 1964
DIAGNOSTIC SESSIONS—DISEASES

Chairman, ASA SEEDS

EMPIRE ROOM

T-7 *"Determination of Amino Acid Active Transport Into Tissue Cells."* W. J. HENDERSON, E. N. BOWSER, G. A. WILLIAMS, (Radioisotope Service, V.A. West Side Hospital, Chicago, Illinois.)

Radioisotopically-labeled non-metabolizable amino acids (especially α-aminoisboutyric acid-C^{14} or AIB-C^{14}) have frequently been used to study amino acid transport into tissue cells under various conditions. In order to accurately determine the presence and the magnitude of active transport, the concentration (C) of AIB-C^{14} must be determined in the intracellular water (ICW) and extracellular water (ECW) of the tissue, and the data expressed as the AIB-C^{14} concentration ratio $\frac{\text{ICWC}}{\text{ECWC}}$. Because of the variability of tissue water compartments among different body tissues and under various experimental conditions, it is advisable to determine the intra- and extracellular space for each specimen of tissue analyzed for AIB-C^{14}. The following method allows all necessary determinations to be made on a single very small tissue

specimen (examples for the rat parathyroid will be given).

AIB-C^{14} and Cl^{36} (the latter to determine extracellular space) are injected. The animal is subsequently sacrificed by exsanguination. Tissue samples are rapidly obtained, sealed in polyethylene envelopes, weighed on a microbalance, and dried in a specially designed desiccator. The dried tissue samples and serum samples are placed in counting vials, digested with Hyamine, mixed with scintillator and the C^{14} and Cl^{36} activity determined in a liquid scintillation counter.

The concentration ratio is calculated as follows:

$$\frac{ICWC}{ECWC} = \frac{\frac{TA-ECW \cdot ECWC}{TW-ECW}}{ECWC}$$

where: $$ECW = \frac{\text{Tissue } Cl^{36} \text{ activity}}{\frac{\text{Serum } Cl^{36} \text{ concentration}}{0.93 \cdot 0.95}}$$

0.93 = Correction for % water in serum
0.95 = Donnan equilibrium constant
TA = Total C^{14} activity of tissue
ICWC = Intracellular water C^{14} concentration
ECWC = Extracellular water C^{14} concentration
TW = Total tissue water

T-8 *"Radiometric Utra-Microanalysis."* Oscar Kanner, (Chief Laboratory and Radioisotope Services, V.A. Hospital, Oteen, North Carolina.)

As early as 1933, Ehrenberg conceived analytical ultra-micro methods based on the use of thorium B (Pb^{212}) and an electroscope for activity measurements. With this simple equipment he designed methods for acidemetry, oxydimetry, iodimetry, as well as for the determination of a number of kations and anions. Today's availability of numerous isotopes and of more refined instrumentation induced us to try to revive Ehrenberg's ideas. We wish to present first the use of Ca^{45} and of Pb^{210} for purposes of acidimetry and alkalimetry. The principle is this: To the acid to be determined a suspension of indicated Ca CO_3 is added to excess. An equivalent amount of indicated Ca or Pb is thus dissolved, and its activity is determined. The relationship between the amount of acid present and the corresponding activity of dissolved labeled lead or calcium was found to be linear over a very wide range.

The method to be presented permits the recognition of differences of amounts of acids down to the order of 10^{-9} equivalents (a millionth of a milliequivalent).

T-9 *"Radioactive Colloidal Gold Measurements Of Lymph Flow In The Extremities."* Harold H. Sage, B. K. Sinha, Dogan Kizilay, and Rudolph Tc̆ylon, (New York University, New York.)

Radioisotope techniques have been devised and standardized in this laboratory (1,2,3,4) which are useful in studying the dynamics and functional pathways of lymph flow together with lymph node pick-up and filtration function. Radioactive colloidal gold (AU^{198}) has been found desirable for this study. Using one injection, a set of observations is made which includes all four aspects. Colloidal gold (15-25 microcuries in 0.1cc liquid) is injected without operative exposure, into the particular lymphatic compartment of the extremity to be studied such as subcutaneous, skin or muscle. Because of its colloidal, metallic nature and size, it is carried entirely in the lymph. Some colloidal gold is deposited in the first station of lymph nodes within minutes. Some is routed to second and third stations of nodes, particularly after the first station is loaded. Colloidal gold which enters a node remains there for the duration of the study, so that deposition of colloidal gold measures filtration function of the node. Lymph nodes of the

extremity filter out most of the colloidal gold. The remainder, however, bypasses all nodes to enter the thoracic duct and blood from which it is quickly cleared by the reticuloendothelial cells of the liver.

Because it is a gamma emitting isotope, AU^{198} can be traced and measured in its passage through the lymphatics and sites of deposition in the lymphatic system by means of external measurement techniques. Because of its halflife, 2.69 days, in vivo, serial, continuous or interrupted quantitative observations can be performed over a period of several days, so that physiologic as well as complex disease states can be studied. Because of the minute amount (0.1cc) used, there is no artefactual distention of lymphatics. The measurements of dynamics and pathways of lymph flow truly represent physiologic and pathologic states studied. This technique has been applied in normal and disease states and an analysis of results will be presented.

T-10 *"Thyroid Uptake In Studies Using Various I^{131} Labeled Preparations."* Y. WANG, (Presbyterian University Hospital, Pittsburgh, Pennsylvania.)

Thyroid uptake of disassociated I^{131} from the original preparation has not been well documented. This information is important in preparing the patient for a specific study and also in evaluating the biological stability of I^{131} labeled preparations. Twenty-four hour thyroid uptakes were determined following adminstration of the commonly used I^{131} labeled preparations. I^{131} triolein thyroid uptakes showed a linear relation with amount of Lugol solution administered. Without administering Lugol solution the range was 18.5%-7.2%; two, three and four doses of 5 drops each in one day, the ranges of uptake were 6.8-3.1%, 2.9-0.2% and 1.0-0.2% respectively. The I^{131} Hippuran thyroid uptake was in the range of 2.6-0.0% (average 0.6%). The I^{131} rose bengal thyroid uptake was in the range of 7.9-0.0% (average 0.9%). The I^{131} RISA thyroid uptake was in the range of 9.0-5.8% (average 6.8%). From these results, the disassociation of I^{131} from the labeled material is almost insignificant in the most cases by intravenous administration, except for RISA and for oral administration of I^{131} triolein which showed a high rate of disassociation. In preparing the patient for I^{131} triolein absorption study, four doses of Lugal solution, five drops each, completed in one day is satisfactory for proper blockage of thyroid uptake of disassociated I^{131}. In the literature, various amounts of Lugal solution from zero to 48 drops in various periods from 1 to 3 days were reported. Following administration of the above mentioned I^{131} preparation, except for I^{131} triolein and RISA, the routine I^{131} thyroid function study can still be carried out with a reasonable degree of accuracy.

T-11 *"Studies With Radioactive Copper In Patients With Wilson's Disease And Their Relatives."* W. NEWLON TAUXE, AND NORMAN P. GOLDSTEIN, Sections of (Clinical Pathology and Neurology, Mayo Clinic, Rochester, Minnesota) With the technical assistance of Dorothy Jenkins, M.T. and Virginia Stellmacher, M.T.

Thirty-eight studies with radioactive copper have been carried out in 10 normal persons, in 10 patients with Wilson's disease and in 10 heterozygous relatives. Radiocopper for 72 hours has been quantitated serially in plasma (including ceruloplasmin), erythrocytes, urine and stools. In addition, serial external counting over the liver was performed.

Including the normal, a total of six distinct kinetic patterns were observed, four of which were seen in patients who themselves had Wilson's disease.

The first would be the normal pattern.

The second was asymptomatic preclinical disease ("coppering state") in which virtually all injected copper accumulated in the liver, with minor spillover into blood, urine or stool.

The third was symptomatic hepatolenticular degeneration ("coppered state"), in which free copper spilled over into the tissues and in which, in the urine, amounts were found which were higher than normal by approximately tenfold.

The fourth was a condition ("decoppering state") in which body stores of patients receiving penicillamine were being depleted and free copper in the urine was found to be higher than normal on the order of a hundredfold.

The fifth was observed among patients temporarily *not* receiving long-term penicillamine therapy ("decoppered state") in whom injected Cu^{64} was found to accumulate in the tissues again with insignificant urinary spillover. This resembles the "coppering" pattern.

A sixth kinetic pattern was that seen in the heterozygous state, in clinically asymptomatic persons all of whom were relatives of patients with Wilson's disease. This state can be separated from the normal on the basis of the ceruloplasmin Cu^{64} incorporation kinetics, by the fecal excretion pattern and by hepatic radioactivity as monitored by external counting.

Possible theories for the various patterns will be discussed.

Since these various kinetic patterns are readily distinguishable by the use of radioactive copper, we have found it important to study the families of patients with Wilson's disease as completely as possible to establish the genetic pattern and also to detect the occasional preclinical "coppering" patient before symptoms occur, so that proper therapy may be instituted.

T-12 *"C^{14} Glucose Kinetics In Diabetes And Acromegaly."* **E. MANOUGIAN, M. POLLYCOVE, J. A. LINFOOT, AND J. H. LAWRENCE, (Donner Laboratory, University of California, Berkeley, California.)**

Glucose tracer kinetics using the single, intravenous uniformly labeled C^{14} glucose technique and continuous monitoring of labeled and non-labeled carbon dioxide have been performed in patients with diabetes mellitus and acromegaly. Previous studies from this laboratory reported similar investigations in normal human subjects and the effects of insulin, tolbutamide and phenethylbiguanide. This study is an amplification of these kinetic studies in patients with juvenile diabetes, adult-type diabetes and acromegaly—many of whom were subsequently treated with heavy particle pituitary irradiation.

A steady-state two compartmental model with unidirectional flow, suggested by Baker et al, was used in the analysis of the data. The parameters which most critically distinguished the patients with abnormal glucose metabolism were: (1) labeled blood glucose halflife (t ½); (2) glucose pool (P_G); (3) glucose pool calculated in gm glucose/Kg of body weight (P_G^W); (4) fraction of the glucose pool which turns over per minute; and (5) required time for the expired breath to reach maximum specific activity (t max). Less critical data were: (1a experimental specific activity of expired CO_2 at t max ($E^{SA}_{CO_2}$(t max)); (2a) milligrams of glucose oxidized to CO_2 per minute (G_{CO_2}); and (3a) oxidation of glucose to CO_2 in g/kg/hr ($G^W_{CO_2}$). Very little differentiation could be seen in the other parameters measured.

Diabetic patients, when not taking insulin or hypoglycemic agents, had a prolonged t ½ (200-600 min), increased P_G (28 gm) and P_G^W (0.38 g/kg), a diminished λ_1 (0.0059 min^{-1}), and a delayed t max 150 min). Some decrease in $E^{SA}_{CO_2}$ ((t max)(0.150) uc/gC) and a G_{CO_2} (64 mg/min) was also seen.

In general the patients with active acromegaly had abnormalities similar to the diabetics but these were less marked and more difficult to distinguish from normal subjects.

Heavy particle pituitary irradiation reversed the abnormal kinetics in the patients with acromegaly but did not appear to affect significantly the abnormal kinetic studies in adult-type diabetes.

THURSDAY AFTERNOON—JUNE 18, 1964

P-1 2:00 PM—PANEL ON SIDE EFFECTS

Moderator—NORMAN SIMON

Radiation, like all drugs, has effects other than those immediately desired. Some of these side effects have received unusual emphasis to the exclusion of the benefits of radiation. In spite of any possible preformed conjectures in any specific field, we should know the milieu in which we work.

H. J. MULLER—*Genetic Effects of Radiation.*

With rare exceptions, a heterozygous mutant gene reduces fitness, though slightly. The number of individuals that ultimately receives the gene before it causes genetic death tends to be inversely proportional to the impairment per individual. "Large" and "small" mutations are therefore, in the long run, equally damaging, and each constitutes one lethal-equavalent. Because of the similarity in the effects of induced and spontaneous mutations, the former are expressed mainly in a higher incidence of mortality, morbidity, and inadequacies of the same types as those prevalent otherwise. The radiation of medical origin received by Americans over the last thirty years must have produced some ½ to 3½ million lethal-equivalents, which will have effects scattered over centuries—a total damage far greater than the somatic damage expressed in the exposed generation. Thus, were it not for genetic damage, higher bodily doses should be permissible. Most genetic damage induced in man could be avoided by artificial storage of germ cells.

CARL F. TESSMER—*Radiation And Carcinogenesis.*

The initial and intervening steps between radiation and carcinoma are being slowly defined. Karysome analysis, now on a practical but not quite routine level, has opened a large segment of this area between initial radiation and subsequent effects, and promises quantitative aspects. Recent studies of in utero irradiation present good statistical evidence (MacMahon) and some speculation (Sternglass).

Evaluation of the carcinogenetic potential of radiation is a constant requirement, with such formidable problems as the long observation period as well as sharpening the interpretation of existing observations. For example, abnormal cellular pleomorphism in the thyroid persists years after radiation, a finding which still awaits some assignment of significance to the patient. As an example of more advanced analysis, the thorotrast story is perhaps the most significant one unfolding in present clinical experience. Recognizable changes may occur at quite low levels of radiation, such as the bilobed lymphocytes described by Ingram following several hundred milli-roentgens, for which no assessment of significance has been made. While radiation carcinogenesis deals largely with somatic cell changes, the germ cell aspects should not be ignored. Carcinogenesis remains one of the overwhelmingly important long term side effects which must be included in all considerations of radiation.

HUGH F. HENRY—*Aging Effects Of Radiation Exposure.*

Radiation exposure apparently causes an aging process which is manifested by effects upon the overall life span and by the early appearance of physiological changes normally accompanying natural aging. Both of these indications will be discussed, primarily from the viewpoint of experimental evidence, although some mention will also be made of current theories. The effects of both short-term and chronic exposures will be mentioned with particular emphasis on some of the difficulties encountered in interpreting the data as well as apparent discrepancies observed. Special attention will be given to the longevity effects of chronic low level exposures.

NORMAN SIMON—*Leukemia Following Irradiation.*

The incidence of leukemia increases in populations receiving large doses of radiation. This observation has been confirmed in the survivors of the atomic bombings in Japan, in radiation-treated patients with spondylitis, and in older radiologists. It is difficult to determine whether low-dose radiation is leukemogenic, but prudence makes us consider it so.

MARSHALL BRUCER—*Radiation Ain't As Evil As You Think.*

Improbable events might or might not appear in small samples. We can generalize medical statistics as being one of four kinds of large samples; but, although most large samples are trivialities, we still have to define what we mean by a large and a small sample. Since most medicine is a "feeling" derived from many small samples by many physicians, a scientist can describe exactly what he sees and still be a liar. The only way to win at dice is to own the crap table.

THURSDAY AFTERNOON—JUNE 18, 1964

P-2 3:45 PM—PANEL ON DIAGNOSTIC ADVANCES

EMPIRE ROOM

Moderator—FRANZ BAUER

Problems of body composition, management of intracellular electrolytes by isotope dilution, total body counting and neutron activation analysis have taken their place in clinical medicine. So have determination of cardiac output, minute volume and coronary blood flow. Experts with a recognized background in their respective fields will discuss these new and important techniques.

PHILIP C. JOHNSON, JR.—*Radioisotope Measurement of Coronary Flow. Comparison Of Methods.*

Relative or absolute coronary flow measurement has been a continuing goal of radioisotope research because conventional methods of measuring coronary flow are not technically convenient for large clinical populations. Three approaches to myocardial flow measurement have been published: ratio of cardiac and cerebral washout slopes, coronary areas ratio formula and cardiac rubidium uptake. Each method has intrinsic problems which have made it unacceptable for clinical investigation. The theory and formulas of each method will be contrasted and compared. Data obtained using two of the methods simultaneously in dog experiments and patients will be presented. Suggestions for further investigation will be made.

WILLIAM F. BETHARD—*Activation Analysis.*

With the advent of improved neutron sources and sophisticated instrumentation, neutron activation analysis has become a powerful analytic tool. Sixty-nine elements in the periodic table can be quantitated by neutron activation with an average sensitivity of 0.01 μg. Attempts are underway to automate the analysis so that results can be obtained without radiochemistry by means of computer techniques. So far this has not been entirely successful; but it shows promise. Neutron activation analysis is particularly pertinent to the study of trace elements in biology. These elements are present in very low concentrations, yet they play very important roles in biochemical processes.

J. THOMAS DOWLING—*Newer Thyroid Function Tests.*

Newer thyroid function tests give emphasis to *in vitro* techniques and have an application to such problems as habitual abortion and liver disease.

WILLIAM H. BLAHD—*Whole Body Counting.*

The whole body counter is an elaborate instrument assembly designed to measure minute quantities of radioactivity in human subjects. These instruments may be used to measure radioactive contamination at below maximum permissible levels. A more specialized field of measurement includes the study of radium or mesothorium poisoning. In the medical field the measurement of radioactive potassium-40, a normal constituent of living cells, provides the basis for important clinical studies relating to total body potassium levels in health and disease, and leading to studies of lean body mass and body fat proportions. Whole body counting also provides a new approach to conventional tracer investigations since such studies can be carried out at tracer levels far below those hitherto used and investigations can be continued for prolonged periods.

THURSDAY EVENING—JUNE 18, 1964

6:00 PM *OFFICIAL COCKTAIL PARTY* GOLD ROOM

7:00 PM *ANNUAL BANQUET* CHURCHILL ROOM

The Annual Banquet will be served on Thursday night, June 18, 1964 at 7:00 PM. A cocktail hour, sponsored by the commercial exhibitors, will precede the banquet at 6:00 PM. A reasonable charge will be made for the banquet, amounting in fact to very little more than a member would pay routinely for his dinner. Considering that the cocktails and the dinner wines will be provided as a courtesy, a member would be out of pocket if he failed to come to the banquet.

The entertainment will consist of background music by Polynesians followed by 45 minutes of Hawaiian and Polynesian dances. There will be an interlude for the presentation of awards and, we hope, the introduction of all past presidents. There will be no formal after-dinner speaking.

FRIDAY—7:30-8:45 AM—JUNE 19, 1964

REFRESHER COURSES

A-6 *Diagnostic Blood Studies*—MYRON POLLYCOVE. (Study A)

Measurements of red cell volume, conveniently performed with Chromium^{51} or P^{32}, are helpful in the diagnosis of polycythemia. Simultaneous plasma and red cell volume measurements, using I^{131} or I^{125}-albumin together with labeled red cells, are useful in the diagnosis of polycythemia, many causes of hyper-or hypovolemia, and as a guide to therapy in hemorrhage and shock.

Vitamin B_{12} absorption measurements using Co^{58} or Co^{57}-vitamin B_{12} may be performed accurately with a whole body counter or hepatic counting with a scintillation detector probe. Other methods involving urine or stool measurements and new functional measurements are made of folic or vitamin B_{12} deficiencies using C^{14} compounds.

Survival of circulating erythrocytes may be determined with Chromium^{51} or DFP^{32}. The latter compound does not elute significantly and may be used for survival studies of granulocytes and platetlets.

Iron and erythrocyte kinetic studies performed with Fe^{59} are helpful in providing a functional analysis of red cell production and destruction including location of the sites at which these occur. This technique is useful in distinguishing between extra- and intramedullary hemolysis and in selecting patients with anemia for splenectomy.

A-7 *Radioisotope Therapy*—HENRY JAFFE (Study B)

A review of the indications, techniques and results of the following radioisotope treatment will be presented:

1. Radioiodine (I^{131}) treatment of hyperthyroidism, euthyroid cardiac disease and thyroid cancer.
2. Colloidal chromic radiophosphate and radiogold for inoperable carcinoma of the prostate.
3. Treatment of chronic cutaneous ulcers with P-32 ointment.
4. Treatment of bone metastasis secondary to carcinoma of the prostate and breast by intravenous radiophosphorus.
5. Treatment of polycythemia vera and chronic leukemia with radiophosphorus.
6. Treatment of cancer effusions of chest and abdomen with colloidal chromic radiophosphate.

A-8 ***The Medical Radioactive Isotopes*—MARSHALL BRUCER** **(Study C)**

There are 276 radioactive isotopes that fit purely physical criteria of being adaptable to medical use. Interestingly enough, the historically first radioisotopes (radium and carbon 14) do not fit the physical criteria. There are too many radioisotopes available to medicine and too much data necessary to the use of each for anybody to remember. Therefore, there has to be a system. Some systems are available and are already in use outside of the fields of medicine.

A-9 ***Effective Audio-Visual Presentation of Data*—JACK FASON** **Gold Room**

The foundations for effective audio-visual presentation of lettered, graphic and pictorial data, including:

1. Concept of the A-V idea.
2. Selection of presentation medium.
3. Art-Work Size Standards.
4. Photography considerations.
5. Projection essentials.
6. Voice and microphones.

A-10 ***The Radioiodine Techniques Of Evaluating Thyroid Function*—ERVIN KAPLAN AND EDWIN B. MILLER** **(Study E)**

This refresher course will be concerned with specific techniques employed in making the measurements necessary to arrive at a quantitative evaluation of thyroid function. The techniques to be studied will be organized in relation to the physiologic cycling of I^{131}, commencing with plasma clearance by the thyroid and kidneys; uptake by the thyroid including anatomical localization by scanning. Intrathyroidal metabolism will be exemplified by effective halflife studies, while post-release aspects of thyroid hormone will be related to determination of protein bound I^{131} conversion ratios and red cell binding of triiodothyronine.

Clearance studies of the labeled hormone from the blood leading to peripheral utilization will complete the series of metabolic events. In addition, specific tests of thyroid stimulation and inhibitation as exemplified by thyroid stimulating hormone and triiodothyronine depression will be described.

FRIDAY MORNING—JUNE 19, 1964

DIAGNOSTIC SESSIONS—WHOLE BODY COUNTING

***Chairman*, GEORGE THOMA**

EMPIRE ROOM

F-1 ***"Simultaneous Studies Of Sodium, Potassium And Water Spaces In Man."*** **GEORGE C. HENEGAR, B. FRITSCH, N. STEFANOVIC AND F. W. PRESTON, (Northwestern University, Chicago, Illinois.)**

A knowledge of the total body sodium, potassium and body water spaces in man permits a better perception of the changes in these compartments in disease and in the post operative state.

With more refined counting devices and the use of simultaneous equations, the three compartments can be measured simultaneously.

Total body sodium was measured with $Na^{22}Cl$, total body potassium with $K^{42}Cl$, and total body water with H_2^3O. Seventeen patients were studied with the three isotopes. Four cirrhotic patients were studied while being prepared for porta caval shunt. Diuretic agents and sodium restriction were used to mobilize water and sodium. All measurements were repeated after the porta caval shunt.

Untreated cirrhotics had markedly elevated sodium space (up to four times normal), moderately elevated total body water, and a low potassium space (to approximately half the normal values). With diuretic treatment and salt restriction, the values for sodium, potassium and water spaces were altered toward but never reaching normal values. After porta caval shunt, the trend is toward high sodium and water space values with a low potassium even while receiving diuretic therapy.

In patient studied pre and post operatively, the sodium and water spaces show an increase following surgery while the potassium is decreased. At about the 10th post operative day, these returned to normal preoperative values.

F-2 *"Clinical Use Of A Whole Body Counter."* THORNTON SARGENT AND HIROSHI SAITO, (Donner Laboratory, University of California, Berkeley, California)

A physician frequently sees anemic patients in whom he suspects blood loss is occurring, but clinical tests for occult blood in stools are not always reliable and are not accurate quantitatively. Bleeding may be intermittent, and thus be easily missed, and collection of samples is an unpleasant procedure for the patient. The whole body counter is capable of accurately measuring blood loss by the very simple and straightforward procedure of injecting Fe^{59} and thus labeling the circulating red cells. By calculating or preferably by measuring the patient's blood volume and hemoglobin concentration, the net decrement of radioiron in the body between two successive visits to the counter can be converted directly to milliliters of blood loss. As we have previously reported, a study of iron loss in ten normal males has established a normal daily blood loss of one to two milliliters. Case examples will be presented of patients with menorrhagia, bleeding ulcers, ulcerative colitis, congenital hemorrhagic telangiectasia, coeliac disease, paroxysmal nocturnal hemoglobinuria, and bleeding of unknown etiology. In some of these cases the bleeding was not documented prior to whole body counting. In others the quantitative information was important to the physician since the rate of iron loss could be calculated to determine maintenance therapy by parenteral iron, or correlated with periods of acute hemorrhage or other clinical symptoms. Interpretation of blood loss curves, however, is not always unambiguous nor straightforward, and cases of this kind will also be discussed.

F-3 *"Gross Body Composition As A Function Of Chronologic Age."* TERUO NAGAI, TAKESHI IINUMA, AND TOMIO ISHIHARA, (National Institute of Radiological Sciences, Chiba, Japan.)

We have already reported "lean body mass" measurements in patients with periodic paralysis by K-40 and tritium dilution. Total body potassium, however, is also of great interest.

More than 200 normal male and female subjects aged 6 to 80 years were assayed for K-40 in the National Institute of Radiological Sciences, Chiba, Japan human counter. The counter has eight 50 x 50 x 15 cm plastic scintillators and thirty-two 5-in-diam. phototubes in an iron room. Subjects were laid on a counting bed outside the iron room after taking a shower and then wheeled between the detectors. Pulses from detectors were analysed by a 2-channel pulse height analyser. K-40 was measured by counting the pulses for a measurement time of 15 minutes.

The counter has been calibrated by the measurement of human body phantoms of a selected size range that contained a known amount of KCl. The lean body mass was calculated from the total body potassium content on the basis of a potassium content of 68.1 meq/kg. Total body fat was calculated as the difference between gross body weight and lean body mass. The "Total Body Water" was derived from the "Lean Body Mass" by using the Pace-Rathbun formula ($LBM = TBW \frac{100}{73}$).

The results showed an interesting dependence on age and sex and were similar to the observations reported by Anderson *et al.* Potassium-40 measurements are valuable in assessing growth, sexual maturity, the effects of exercise, aging and senility.

F-4 ***"Radioisotope Pulmonary Function—Studies With Xenon-133."*** **GERALD L. DENARDO, MAJOR, DONALD J. BOWES, CAPTAIN, JEROME S. BRODY, CAPTAIN, JON B. GLAZIER, CAPTAIN, (Fitzsimons General Hospital, Denver, Colorado.)**

Xenon-133, an inert radioactive gas with a halflife of 5.27 days and a gamma radiation of 81 kev, is suitable for in vivo studies of pulmonary ventilation and perfusion.

Four motor-driven detectors, one over the anterior and one over the posterior aspect of each lung, with 3 x 2 inch crystals and 3 x 1 inch rectangular collimators, scan the lungs to determine the quantity of radioactivity over an infinite number of points. The pulses from each detector pass through a pulse height analyzer and are recorded on a 20 channel magnetic tape recorder, which also records from a spirometer the amount of gas the subject inhaled. Each channel is played back through a ratemeter and recorded on an X-Y plotter resulting in a count rate profile for each lung. This procedure is repeated during the course of normal breathing, equilibrium breathing, perfusion, wash-in, and wash-out of Xenon-133.

This information is recorded on the magnetic tape in tabular fashion, rather than sequential fashion. This arrangement permits the use of electronic circuitry to manipulate the information. The information from any two channels can be added, subtracted, multiplied or divided prior to recording on the X-Y plotter. This is particularly useful in providing the ratio of ventilation-perfusion from each detector. This is the most important single item of information, since there is presently no non-radioisotope technique for measuring this relationship on a regional basis.

A digital computer is used to assist in data analysis. Several illustrations of normal and abnormal studies will be presented. (Instrumentation, technique and results will also be displayed in a scientific exhibit.)

FRIDAY MORNING—JUNE 19, 1964

THERAPEUTIC SESSIONS

Chairman, MILO HARRIS

EMPIRE ROOM

F-5 ***"Brachytherapy—Past, Present and Future."*** **D. E. KAHLSON, (Atomic Energy Commission, Oak Ridge, Tennessee.)**

The author defines brachytherapy and discusses some of its early history including the initial work done by Marshall Brucer in Oak Ridge. The author points out the need for introducing greater simplicity into modern radiotherapy equipment and suggests that brachytherapy could be developed into a valuable tool for the modern radiotherapist. It is pointed out that brachytherapy utilizes fractions of curies to accomplish the same results as thousands of curies in the treatment of cancer.

Emphasis is placed on the need for a more intensive joint effort by the engineering, scientific and medical professions to design more practical modern isotope therapy apparatus. Properly organized, a joint interdisciplinary team could exploit the full technological potential that exists in each participant's state of the art.

Two brachytherapy applicators are described that would utilize liquid isotopes and permit rapid and accurate evaluations of dosage distributions on a much simplified basis. The applicators would be cheaper, safer and more reliable than most equipment currently available with the additional feature that large groups of specialists would not be required to administer treatment.

The author cites comparable accomplishments in other fields of science and technology which serve to point out the undeveloped potential in the field of practical radiotherapy.

F-6 *"Therapy Of Solitary Nodule In Thyroid With I^{131}."* MARION F. MAGALOTTI, ROBERT J. BECKER, IRVING F. HUMMON, (Radiation Center, Cook County Hospital, Chicago, Illinois.)

The study shows that a patient may have a normal 24-hr., I^{131} thyroid uptake without evidence of hyperthyroidism, but still may have significant demonstrable pathology within the thyroid gland that can be effectively treated with radioiodine (I^{131}). These patients have cardiac manifestations and since the 24-hr., I^{131} uptake is normal, they are not infrequently dismissed from the radioisotope department. We wish to show that it is important to know not only the function of the entire gland, but also of small parts of the thyroid. There may be a thyro-cardiac factor within the thyroid that is only minute in size and not palpable clinically, or a nodule palpable or even visible to the physician.

The abnormal focus within the thyroid gland can be demonstrated with a simple scan, and show hyperfunctioning elements. The rest of the thyroid may be suppressed by the hyperfunctioning focus. After I^{131} therapy, the abnormal focus may disappear or decrease in size with more uniform uptake throughout the thyroid. Although the 24-hr. I^{131} uptake of the thyroid may show little change after I^{131} therapy, the morphological pattern of the thyroid may show much change on the scan.

The importance of decreasing or destroying these hyperfunctioning nodules is to decrease or eliminate the thyro-cardiac factor. We have treated 25 patients that had normal I^{131} uptakes, but the scan showed an abnormality. After I^{131} therapy, the cardiac manifestations, both subjective and objective, have disappeared or greatly improved.

F-7 *"The Use Of Intra-Arterial Chemotherapeutic And Radioisotopic Agents In Treating Cancer Of The Liver."* IRVING M. ARIEL, AND GEORGE T. PACK, (Pack Medical Foundation, New York City.)

This presentation shall discuss the effects of the administration of chemotherapeutic agents (phenylalanine mustard, nitrogen mustard, methotrexate, and others) by the intra-arterial route for primary and metastatic cancer to the liver. In addition, the use of radioactive isotopes, in the form of radiating microspheres containing Yttrium-90 (Y^{90}), administered either into the hepatic artery or interstitially, will be be described. Experiments with combined chemotherapy and radioisotope therapy will be presented. Techniques of administration include, the intra-aortic with an ordinary catheter, the intra-aortic using a Dotter-Lukas catheter, and administration into the hepatic artery via the gastroepiploic artery, will be described. The scans of the liver before and after treatment will be shown and experience with 40 patients treated by this regime will be presented.

F-8 *"Localization of Purified I^{125}-Antitumor Radioantibodies In Human Brain Tumors."* EUGENE D. DAY, M. STEPHEN MAHALEY, BARNES WOODHALL, AND FELIX PIRCHER (Departments of Microbiology and Immunology, Neurosurgery, and Radiology, School of Medicine, Duke University, Durham, N.C.)

Based upon methods worked out in animal systems (Day, Prog. Exptl. Tumor Res. 4:57-97, 1964), the present study has for its objective the delivery of diagnostic and therapeutic amounts of radioactivity to recurring human gliomas through the use of a specific antibody carrier. A necessary adjunct to the study is the delineation of the vascular efficiency of individual gliomas through the use of radioantibodies to the vascular antigens of the tumors.

Individual gliomas are obtained after primary craniotomy, and used as immunizing antigens to prepare antibodies in rabbits and later as a medium for the purification of radioantibody. To date thirty gliomas and antisera against them have been obtained. Individuals

with recurring gliomas, usually about six months after initial surgery, who are suitable candidates for secondary craniotomies, receive an intracarotid injection of 200 microcuries of purified homologous I^{125}-antibody. External brain and total-body scanning are carried out for a few days prior to surgery; gross spectrometric scintillation counting of tumor, normal brain, and blood are made immediately after surgery; and radioautographs of histological sections of all surgical specimens are subsequently obtained. To date five individual studies have been made. Unequivocal localization due to antibody was obtained in two cases; borderline localization (as compared with I^{131}-RISA), in two; and none, in one. To our knowledge this is the first report on the successful localization of truly antitumor antibodies (in contrast to antifibrin) in a human tumor system.

Scans, gross-counting data, and radioautographs will be presented in support of these conclusions, and the problems that require solution before the objective can be obtained will be discussed.

FRIDAY MORNING—JUNE 19, 1964

11:15 AM—*BUSINESS MEETING*

THAD P. SEARS, PRESIDENT

The business meeting will be held Friday morning, June 19, 1964. The committee on nominations will report, the election conducted and the routine business of the Society discussed. An important item is the adoption of the bylaws revision. All members have a revised copy.

It is easy for the membership to bypass the annual administrative meeting, feeling that the officers will carry on and the business of the Society be accomplished without their personal attention. Our major aims are scientific. But no society achieves its scientific objectives unless supported by sound administration. The amount of background work to be done is incredible. The Society needs unity. One of the very best ways to obtain unity is to have every member at the business meeting to discuss administration matters and assist in the formulation of future policies.

FRIDAY AFTERNOON—JUNE 19, 1964

P-3 1:45-3:15 PM—PANEL ON THERAPEUTIC ADVANCES

GOLD ROOM

Moderator—PAUL MEADOWS

Four outstanding investigators will present evidence to support the usefulness of radioactive therapy as the treatment of choice in patients with various malignancies. Dr. Lawrence and Dr. Osgood will discuss radioactive phosphorus in chronic leukemia and polycythemia. Dr. Maxfield will detail his experiences with radioactive phosphorus in the palliative management of bone metastases from carcinoma of the breast and prostate. Dr. Flocks will support the usefulness of interstitial colloidal radioactive gold in certain types of prostatic cancer. An open discussion will follow the presentations.

JOHN H. LAWRENCE—*P^{32} In Polycythemia And Leukemia.*

It has been over 25 years since we did tracer studies in leukemic animals leading to the use of P^{32} and other isotopes in the treatment of leukemia and polycythemia vera. Since then we have treated over 600 patients. The experience in polycythemia vera shows that this disease can be successfully controlled. The life expectancy for these patients is about the same as that for treated diabetes or pernicious anemia, the median age at death being 69 years. In our total series of 167 chronic lymphocytic leukemia patients, 20% have survived over ten years after onset. Thirty-one of these patients are alive today, 15 of them in the interval

of 10 to 27 years after onset of symptoms. Where facilities are available for therapeutic administration of P^{32} and adequate followup, it has also proved to be a simple and highly acceptable means of treating chronic leukemia.

EDWIN W. OSGOOD—*P^{32} In Leukemia And Polycythemia.*

The results of regularly spaced, titrated P^{32} treatment of 303 consecutive patients with chronic leukemia and of 101 with polycythemia vera started on P^{32} therapy between January 1, 1947, and December 31, 1954, compare favorably with results of other methods of treatment. Among conclusions for which evidence will be presented are: polycythemia is not a malignancy; risks of acute leukemia are widely different in polycythemia and lymphocytic leukemia, and the important variables as far as within group prognosis are sex and age. Males and the older half have the shorter survival. Notwithstanding radiation therapy, more than 45 per cent of the 201 lymphocytic leukemia and 38% of the polycytemia patients lived past age 70.

RUBIN H. FLOCKS—*Prostatic Carcinoma.*

2800 patients with prostatic cancer were followed 5 years or more. Of these, 460 patients were treated by interstitial irradiation with colloidal solution of radioactive gold. This was used as an adjuvant in the management of prostatic cancer. The present technique, the complications and the results of this therapy will be outlined.

In addition to the 460 patients followed over a five-year period, we have another 200 patients seen from 1958 to the present time who have given us interesting information with regard to the value of this therapy.

J. R. MAXFIELD, JR.—*P^{32} In Metastatic Ca Of The Breast.*

Beneficial in relieving pain and causing reparative changes, the technique is easy to administer, side effects are minimal, and failure of palliative response is small. The use of this technique in alleviating the pain and rehabilitating the patients in these categories will be stressed, with a comparison between this technique and others. The long time survivals (five years or more) are not high, but those from other methods of treatment are either much lower or do not exist. The claim for this technique is that it is the best palliative technique for the patient with metastatic cancer in bone from breast or prostate; it is not designed as a curative technique.

FRIDAY AFTERNOON—JUNE 19, 1964

P-4 1:45-3:15 PM—PANEL ON SPACES AND VOLUMES

EMPIRE ROOM

Moderator—GRANVIL KYKER

Spaces and *volumes* are such inclusive terms in their connotation of physiological geometry that selection becomes the first question. In nuclear medicine, isotopic tags should serve as a tape measure, assisted by excluding a prominent approach, the art of scanning. A survey sampled each chapter of the Society with a good response and considerable duplication.

The final structure of this panel touches four basic corners of active experimental interest. The first inscribes a large tissue always diffuse, sometimes controversial, and never delineable, like a liver or tumor, by scanning. The second corner is ionic and is occupied by an ion that had only meager status before its radioisotopic debut. The third corner is a complex ionic area and emphasizes hard tissues for which no ordinary tape measure is either adequate, convenient, or comfortable. The fourth corner is the shadow out of which questions should appear; it illustrates stresses that affect measurements, radiation and function tests.

GERSON T. LESSER AND J. MURRAY STEELE—*Tracer Gases To Measure Total Body Fat* In Vivo.

The concept of a fat-free lean mass (FFLM) involved consideration of the mammalian body as the sum of: (a) the body fat, which varies from individual to individual and also in a given individual depending upon current nutrition; and (b) the FFLM, of relatively constant weight in a given healthy adult and of relatively constant composition in all adults of the species. If an independent method for determination of total body fat (ether-extractable material) is available, subtraction of this value from total body weight provides an accurate measure of FFLM. With simultaneous measure of any component of the FFLM—total body water or its subdivisions, exchangeable K, etc.—the proportion of this component of the FFLM can be directly calculated. This calculation permits study of changes in the FFLM with age or disease processes.

Measurement of the volume of an inert, highly fat-soluble gas (cyclopropane) absorbed from a closed respiratory system of known fixed volume proved satisfactory for the determination of total body fat in living rats ($\pm$ 5% compared with extraction of dried tissues with ether) and in human subjects. In humans, due to the slower equilibration of the gas with body tissues, it was necessary to extrapolate observed absorption data to obtain equilibrium values and, from these, values for body fat. The method should enable measurement of total body fat with other inert, fat-soluble gases, and Kr has also been successfully used for this purpose. At present, preliminary studies with Kr^{85} appear to provide similar results to those obtained with stable Kr^{84}. Two groups of normal human subjects—below 40 and above 60 years of age—have been studied for total body fat (cyclopropane and/or Kr), total body water (dilution of HTO) and extracellular space (dilution of $S^{35}O_4$). Significant age-associated changes have been demonstrated in the distribution of water between intra- and extracellular compartments.

JERRY K. AIKAWA—*Studies of Exchangeable Magnesium In Man.*

Mg^{28} ($T_{1/2}$ = 21.3 hr., with high energy beta and gamma emissions) was injected intravenously in tracer doses and plasma clearance, urinary excretion, tissue uptake and specific activities were determined. After about 18 hours, the specific activities in plasma and urine showed only a slight gradual increase, suggesting that the infused material had equilibrated with the stable magnesium in a rather labile pool, and that further exchange was occurring very slowly in a less labile pool consisting primarily of bone and muscle. The labile pool in normal subjects ranged between 2.6 and 5.3 mEq/Kg. of body weight, less than 16 per cent of the total body content of magnesium.

I. S. EDELMAN—*Isotopic Exchangeability And Osmotic Activity.*

Previous studies indicate that radiosodium exchanges incompletely with bone sodium and that radiopotassium exchanges slowly with brain and erythrocyte potassium. The content of bone sodium exchangeable with radiosodium is in excess of any reasonable estimate of osmotically active sodium based on analysis of bone water. These findings may be interpreted to mean that some sodium and potassium are bound to polyelectrolytes (intracellular as well as extracellular) and are partially inactive osmotically. Cryoscopic measurements of the activity of intracellular water, however, are consistent with the concept that cellular monovalent cations are completely dissociated and that water is passively distributed between fluid compartments in man and other mammals. A linear correlation between serum osmolarity and the ratio of the sum of exchangeable sodium and potassium to total body water, found in an earlier study, supports the concept of osmotic equilibrium and of complete disassociation of intracellular cations. A discussion of isotopic exchangeability of sodium and potassium will be presented from the standpoint of relationships to osmotic activity.

Louis V. Avioli—*Radiation Effects On Space Function Tests.*

The acute effects of therapeutic abdominal radiation on renal function have been evaluated in ten patients with intra-abdominal or retroperitoneal malignancies by means of control measurements before, during and following the radiation period. All patients had normal renal function prior to radiation.

The most significant renal effect of radiation was on the renal plasma flow (RPF), which fell progressively during radiotherapy beginning at 400 rads. It proved to be the most sensitive and consistent index of radiation damage.

Transient depressions in the glomerular filtration rate (GFR) at 400 rads were followed at 550 to 1,625 rads by increases above the initial values before radiation. At cumulative dosages of 2,000 to 2,400 rads a progressive decrease in glomerular filtration rate was observed which has persisted up to twelve months after radiation.

Tubular function, measured as the maximum excretory capacity for par-aminohippuric acid (Tm_{PAH}), was more variable but a major trend was a decrease during and following radiation.

No definite alterations were observed in the results of commonly employed laboratory tests of renal function during and following the radiation period. There were no changes in blood pressure, and no clinical evidences of altered renal function in the ten patients studied.

FRIDAY AFTERNOON—JUNE 19, 1964

3:30 PM, FIFTH ANNUAL NUCLEAR PIONEER LECTURE

EMPIRE ROOM

HONORING

LORD RUTHERFORD OF NELSON
(1871-1937)

L-1 Well over 100 years before The Society of Nuclear Medicine, the Prince Consort in England had organized the Great Exhibition of 1851 (the First World Fair). A large profit was made and turned over to bringing scholars from outlying countries to study at British Universities. In 1894 there were two candidates from New Zealand. The first candidate to be offered the appointment got married and so the second candidate, Ernest Rutherford, went to Cambridge University in 1895, to be one of the first science scholars under Professor J. J. Thomson at the Cavendish Laboratories. One of Rutherford's hobbies was photography. In the hands of Crookes and Becquerel, this was one of the main methods for studying radiation. Rutherford never pursued the photographic method because of a second interest—the use of Hertzian waves. His work on wireless communication—even as a student—was simultaneous with the work of Marconi, J. J. Thomson, whose primary interest was in the basic characteristics of electricity, shifted Rutherford from Roentgen's photographic demonstration of the emanation to an investigation of the phenomena connected with the "electrical" effects of uranium and thorium. This led to the discovery of "transmutation", then isotopes, then the theory of the atom, then nuclear physics. In 1898 Rutherford became professor of physics at McGill University, in 1907 he transferred to Manchester University and in 1919 he succeeded J. J. Thomson as head of the Cavendish Laboratories at Cambridge University. Everything in nuclear medicine begins with Rutherford.

L-2 Norman Hilberry, Ph.D.

The Fifth Annual Nuclear Pioneer Lecture of our Historical Series will be delivered by Norman Hilberry, Ph.D., at 3:30 p.m. on Friday, June 19, 1964. The honored scientist will be Ernest Rutherford (1871-1937).

A special commemorative brochure providing a complete biography of Lord Rutherford and Professor Norman Hilberry will be distributed at the 11th Annual Meeting. Dr. Hilberry is presently Professor of Nuclear Engineering at the University of Arizona in Tucson and recently retired as Director of the Argonne National Laboratory. Dr. Hilberry was associated with the group under Professor Fermi which first achieved a self-sustained controlled nuclear chain reaction on December 2, 1942. Dr. Hilberry was instrumental in the establishment of the Oak Ridge Institute of Nuclear Studies and the Brookhaven National Laboratory.

He received his A.B. degree from Oberlin College and his Ph.D. degree in Physics from the University of Chicago. He has been granted the LL.D. degree by Elmhurst College and by Marquette University and the Doctor of Science degree by Monmouth College. He has contributed widely both to science teacher programs and to youth science activities. Dr. Hilberry has devoted much of his attention to the educational responsibility of the governmental agencies in particular those of the United States Atomic Energy Commission. He organized and served as the first Director of Argonne's International School of Nuclear Science and Engineering. Dr. Hilberry served as the leader of the International Atomic Energy Commission's first field mission. He is a member and has served as an officer of many professional societies.

SATURDAY—7:30-8:45 AM—JUNE 20, 1964

REFRESHER COURSES

A-11 *Clinical Laboratory Equipment*—Theodore Fields. (Study A)

There are problems besetting the clinical radioisotope user in selecting equipment for his laboratory. Especially in the small office and small hospital he must evaluate such items as sensitivity, accuracy, reliability, convenience and economics against a piece of equipment that must have a detector, support, shield, receiver and read out-system.

The discussion will concern the most commonly employed procedures in radioisotope diagnosis and therapy. Suggestions will be made about the routine calibration and maintenance of the devices. Arguments for and against solid-state devices will be presented.

A-12 *Effect of Radiation On Tissues*—I. Meschan, D. J. Pizzarello. (Study B)

I. Sequence of events following irradiation in relation to time consumed.
   A. Graphic representation of what happens following exposure to radiation.
II. The concept of Linear Energy Transfer and Mass Energy Transfer (LET and MET).
III. The initial chemical lesion in cellular radiobiology.
   A. The target theory.
   B. Relative biological effectiveness and its measurements.
VI. Effects at the cellular level.
V. Biochemical mechanisms for cellular effects.
VI. Effect of oxygen in radiobiology.
VII. Comparative radiosensitivity of various tissues.
VIII. Presentation of slides demonstrating summary radiation effects on tissues by internal and external radiation.
   A. Shortening of life span, leukemia induction, cataract formation, damage to the embryo.

A-13 *The Measurement Of Radiation Coming From A Patient*—Douglas A. Ross. (Study C)

Two general situations arise:

1. You *give a radionuclide* to a patient; after a suitable interval you investigate its distribution, or measure its concentration in a metabolically involved organ.

2. *He has acquired a radionuclide by accident;* can he eliminate it from his system unaided, and if not, does it threaten his health or life?

The pitfalls associated with counting geometry, tissue absorption, scattered radiation, and pulse-height selection will be discussed, and suitable evasive tactics suggested. The special difficulties arising during very low-level whole-body patient counting will then be considered, and several illustrative "whole-body spectra" shown. The principles involved will be illustrated with pictures of typical external counting systems, linear scanners, area scanners, and whole-body counters.

A-14 ***Statistics Of Radioisotopes*—V. P. COLLINS, C. A. PEABODY, R. M. ADAMS. (Study D)**

After a simple notation is established and the necessary definitions and formulas presented, the Poisson distribution and the elements of sample theory will be presented briefly. Development will be by way of discussion, analysis and solution of common problems, e.g., what is the relation between the number of counts recorded and the activity in a sample, at various levels of counting rate? What is the effect of changing a threshold setting in a counter? How can the presence of two radioisotopes be dealt with?

Finally, how can an understanding of the statistics involved help in presentation of data and in calculations of radiation dose?

A-15 ***The Radioisotope Technique Of Determining Blood Volumes*—R. W. DIELMAN, P. J. O'REILLY AND GEORGE M. ANDREWS, SR. (Study E)**

The radioisotope technique for determining blood volumes by separate or simultaneous methods utilizing radioiodinated human serum albumin for plasma volume, and radioactive chromium for the erthrocyte volume, will be presented.

The technique of isotope dilution by tagging and sampling the medium, permits the calculation of volumes. However, no "volumes" could be more difficult to determine than blood volume, due to its irregular shape and sometimes only semantic reality.

In conclusion, the procedures, their sequence and the values of measurements obtained will be outlined in this course as they relate to the determination of accurate and reliable blood volumes.

SATURDAY MORNING—JUNE 20, 1964

PRECLINICAL SESSIONS

Chairman, NORMAN J. HOLTER

EMPIRE ROOM

S-1 ***"Design and Properties Of The Duke Whole Body Counter and Scanner."*** **A. P. SANDERS," F. J. PIRCHER, AND T. BUFFALO, (Duke University, Durham, North Carolina.)**

Design: The instrument represents an advancement of the ORINS Linear Scanner. It has 10 detectors, each with a 2 × 2 inch scintillation crystal. The detectors are arranged in five channels across a motor driven table on which the patient is placed. The detectors are collimated with 2 inches of lead along the assembly and with 1-inch partitions in between the detectors. The 2-inch collimation is variable. The output from each pair of the detectors is fed into a pulse height analyzer and from there into a pair of scalers and, finally, into a print-out typewriter. The scalers print and count alternately. They record the digital data in 5 channels along the length axis of the patient's body. The scalers are advanced by a microswitch which makes contact every 2.3 centimeters the table moves. In addition, all 5 channels are fed into a rate meter recorder which gives a profile recording of radioactivity.

Properties: The efficiency of the detectors and the iso-response curves were determined for each channel for various collimator openings. The results show adequate definition of cross sections and some definition between the 5 channels. The phantom experiments indicate that the efficiency of whole body counting is adequate for clinical work. The resolution is not as good as the one provided by focusing collimators, but adequate for gross localization and quantitative determination of distribution.

S-2 *"A Diagnostic-Level Whole-Body Counter."* A. C. Morris, Jr., (ORINS, Oak Ridge, Tennessee)

A whole-body counter measuring an activity range from 100 microcuries down to 0.1 microcurie is in clinical use. Radiation detection is accomplished by means of four 3- x 3-in. scintillation crystals mounted in a collimating lead trough 1¼ in. thick and weighing 3000 lb. The trough-like collimator allows all the crystals to view the entire length of the patient, and all detected counts are summed into one input for the spectrometer system. The subject reclines on a special type of X ray stretcher, which is radiolucent and is pushed over the collimator-detector assembly where the count is made. This counter has the advantage that it operates in the same activity range as that of many clinical isotope studies and whole-body counts may be performed concurrently with these studies.

S-3 *"Whole Body Counting Of Non-Uniformly Distributed Radioisotopes."* S. Genna, M.S., W. Dukstein, R. Jones, and B. Burrows, (Evans Mem. Dept. Clin. Res., Mass. Mem. Hosp., Dept. of Med., Boston U. Med. Center, Boston, Massachusetts.)

A whole body counter used to determine retention of a radioisotope should permit body radioactivity to be measured independently of radioisotope distribution or body size. This paper reports an improved method of counting non-uniformly distributed radioisotopes in man.

The body counter consists of two 4 × 8 inch NaI (Th) crystals suspended above a bed in a steel room of 9 inch average thickness. The crystals are positioned one meter apart at 45° angles and 73 cm above the bed. The subject is counted in the supine and prone positions. Of the crystal arrangements considered, this array is least sensitive to changes in photopeak count rates resulting from different distributions of radioactivity in the body. However, significant variations remained.

Studies using tissue-equivalent phantoms were made to derive an empirical correction for the remaining variation. The correction utilizes the relative magnitude of the counts in two separate regions of the spectrum. These are the photopeak region and a lower energy band arising primarily from forward Compton scatter of the primary photons. This correction when

Studies in human subjects with labeled compounds that localize in various body sites show uncorrected photopeak count rate variations of up to 25% resulting from changes in distribution alone. Application of the correction reduced the variation to ± 4 per cent.

S-4 *"Scintillation Scanning With An Eight-Inch Diameter Sodium Iodide Crystal."* JOHN G. MCAFEE, J. M. MOZLEY AND H. N. WAGNER, JR., (The John Hopkins Medical Institutions, Baltimore, Maryland.)

In scintillation scanning with crystals three inches in diameter, resolution has been limited as much by statistical variations in count rate as by the optical resolution of the collimators. Furthermore, the excessive time consumed for each procedure has prevented the widespread application of scanning to large numbers of patients.

An instrument was constructed with an eight-inch diameter crystal mounted below the table top and with a remote X-Y plotter for photo-recording. The sensitivity of detection was improved by a factor of 6 compared with three-inch crystals, and by a factor of 2 compared with five-inch crystals. For comparable doses of radionuclides administered, the time required for scanning procedures could be greatly shortened. This was particularly advantageous for cerebral and pulmonary scanning. Alternatively, the resolution could be improved for the same interval of scanning time. This enabled the detection of smaller lesions of the thyroid and kidney. Linear scanning speeds of 48 inches per minute or greater were used.

The problems of pulse height resolution, background shielding and detector transport for an eight-inch crystal will be discussed.

In a series of patients, comparative studies performed with both three-inch and eight-inch crystal scanners will be shown.

S-5 *"Digital Scintillation Scanner."* C. P. ALFREY, JR., J. R. RISER AND V. COOK, (Radioisotope Service, V. A. Hospital, Houston, Texas)

An entirely digital scintiscanning device has been developed. This device consists of a scaling strip from which the number of counts received during any prescribed period may be photographically recorded. In its usual mode of operation a counting period between 0.3 to 3 seconds is used. At the end of a counting period the number of counts recorded on the scaling strip is flashed on to a photographic film (.01 secs.). At the end of the flash the scaler is reset to 0 and another counting period begins. The number recorded on the photographic film is 2×3 mm, a size which can be easily read but which allows recording of 6 intervals per cm^2.

This equipment is so designed that every 4th, 10th, or 40th count may be directed to the scaling strips and from one to four digits may be recorded for each period. In addition, a means of background substraction has been incorporated.

This recorder has been used to record scintiscans of the thyroid, kidney, liver and brain. A digital scintiscan recorder has the following advantages over analog devices: (1) the data is presented in a digital manner and therefore each period is independent of the occurrences in the preceding period, and (2) the data is in a form which can be evaluated statistically.

S-6 *"The Depth Of Focus Of Converging Collimators."* BENEDICT CASSEN, (University of California, Los Angeles.)

In the extreme limiting cases of (1) a single channel collimator and (2) a completely spherical symmetric converging collimator, it is obvious that the first, no matter how much resolution it is designed to give in a horizontal plane, has no vertical resolution. The second, on account of spherical symmetry must have the same resolution in all directions. An analysis is presented of the vertical resolution of a finite angle converging collimator as it depends on the semiangle of the collimator. The vertical resolution increases rapidly with the semiangle of the collimator. The theoretical results are compared with the experimental results obtained using a point source of mercury-203 with a large angle, up to 60° semiangle, 2,200 hole spherical cap collimator. The vertical resolution, when the full angle is used, is not much worse than the horizontal resolution. The depth of focus varies approximately as $(1\text{-}\cos\theta)/(\theta - \sin\theta\cos\theta)$ where θ is the semiangle of the converging collimator.

A discussion is given of the practical possibilities of scanning in a sequence of vertically separated horizontal planes, especially in establishing positions of brain tumors.

SATURDAY MORNING—JUNE 20, 1964

RADIOBIOLOGICAL SESSIONS

Chairman, TITUS EVANS

3:15 PM

S-7 *"Dextran Infusions And Extracellular Volume."* MARCUS A. ROTHSCHILD, MURRAY ORATZ AND SIDNEY S. SCHREIBER, (Radioisotope Service, V. A. Hospital, and Dept. of Medicine, N.Y.U. School of Medicine, New York.)

Plasma volume expansion clearly follows dextran infusions, but little is known concerning the effects of dextran on extracellular volume. The plasma volume and extracellular volume of the body and liver were determined in 15 control rabbits and in 15 rabbits receiving 1.0 to 1.5 g dextran daily (av.mol.wt. 184,000) for 14 days. Rabbit Albumin-I^{131} was employed to measure the plasma volume, and extracellular volume was determined using C^{14} sucrose. The rabbits were sacrificed and the livers removed within 1-1½ minutes following the last blood sample. Hepatic plasma volume and extracellular volume were determined from the ratios, I^{131} and C^{14} per g of liver ÷ I^{131} and C^{14} per ml plasma respectively. Dextran infusions resulted in an increase in the body's plasma volume from a mean control value of 3.4±0.1 to 4.1±0.2% body weight but no change in extracellular volume occurred. The mean hepatic extracellular volume increased from 21.8±0.9% to 24.9±1 % wet liver weight due entirely to the increase in the hepatic plasma volume. No change in interstitial volume was noted. The present studies demonstrate that while the plasma volume for the body and liver increased significantly, there was no change in interstitial volume during dextran infusions.

S-8 *"Non-Dialyzable Manganese And Copper Levels In Human Urine."* EUGENE L. KANABROCKI, LAWRENCE CASE; T. FIELDS; CLARENCE DECKER, ERVIN KAPLAN, (Radioisotope Service, V. A. Hospital, Hines, Illinois.)

Studies of non-dialyzable trace elements, manganese and copper, in serum (1) and in cerebrospinal fluid (2) prompted investigation of these elements in human urine. Purpose of this study was to establish levels of non-dialyzable Mn and Cu in urine of normal and abnormal subjects by means of neutron activation technique.

Sixteen apparently healthy male subjects varying in age from 5 through 47 years were used in this study. Each of the subjects collected four 24-hour urine specimens. Creatinine determinations were performed on these urines to ascertain validity of daily collection. One ml aliquots of each urine were dialyzed and analyzed by neutron activation procedures described previously (1). The mean non-dialyzable urine excretion of maganese was 0.98 ± 0.46 μg per day while that of copper was 54.66 ± μg per day.

Forty-seven 24-hour urines were also collected from 10 hospitalized male subjects and analyzed for these elements. Diagnoses of these patients were: Myocardial infarction, carcinoma of the bladder, Wilson's disease, cirrhosis and schizophrenia. Creatinine analyses were also carried out on these urines. The mean value obtained for daily urine excretion of non-dialyzable Mn and Cu were 3.15 ± 1.31 μg and 137.68 ± 48.26 μg respectively.

S-9 *"Albumin I^{125} Macro-Aggregates For Brain Scanning. (Experimental Basis and Safety)"* G. V. TAPLIN, J. C. KENNADY, M. L. GRISWOLD, M. M. AKCAY, AND D. E. JOHNSON, (Laboratory of Nuclear Med. and Radiation Biology, UCLA Med. School, and Dept. of Radiology, Los Angeles County Harbor General Hospital, Torrance, California.)

Albumin I^{125} macro-aggregates (20-100 μ) are trapped in the dog's cerebral capillaries for sufficient time ($T_{½}$ = 30-60 minutes) following internal carotid artery injection to scan one hemisphere of the brain. These large fragile particles are fragmented in the brain and re-enter the circulation. Surface, as distinguished from deep seated lesions, cause areas of diminished radioactivity in scans performed with the low energy I^{125} labeled particles. Thereby, the scan has potential diagnostic value in localizing superficial lesions which are more amenable to surgical treatment. Radiation exposure is less than 10 mrad to the target organ.

Brain scans in dogs and primates prove the feasibility of the procedure. Physiological, histological and behavioral studies following single and repeated scans indicate a considerable margin of safety. Patients with metastatic brain lesions or inoperable tumors are to be given initial clinical trials.

S-10 *"Absorption of Zn^{65} In Man And Effect Of Dietary Factors Thereon."* HERTA SPENCER, ISAAC LEWIN AND JOSEPH SAMACHSON, (Metabolic Section, V. A. Hospital, Hines, Illinois.)

The metabolic interaction of zinc and other metals, particularly of large amounts of calcium, has been shown to result in various abnormalities in animals. The mechanism by which the unavailability of zinc is induced in animals receiving a high calcium intake is unknown. Little information is available in man on the absorption of zinc from the intestine, and of dietary factors thereon. The absorption of zinc from the intestine in man was investigated on the Metabolic Research Ward under controlled dietary conditions. Tracer doses of Zn^{65} were given orally during low and high calcium intake and the Zn^{65} levels in whole blood, plasma, urine and stool were determined. The variability of absorption of Zn^{65} in different persons as determined from the plasma levels and fecal excretion during the same calcium intake does not seem to be age dependent. The main pathway of Zn^{65} excretion is the intestine. The endogenous fecal Zn^{65} excretion continues for a prolonged period of time and this excretion is higher than the urinary Zn^{65} excretion. An approximate 10-12 fold increase in oral calcium intake did not result in a significant decrease of intestinal absorption of Zn^{65} in man. The effect of different protein intake levels on Zn^{65} metabolism was also investigated.

S-11 *"Chromosomal Abnormalities Fourteen Years Following Treatment Of Thyrotoxicosis With I^{131}."* M. M. NOFAL, A. AL-SAADI, AND W. H. BEIERWALTES, (University Hospital, Ann Arbor, Michigan.)

Chromosomal abnormalities have been described in cultured leukocytes shortly after I^{131} treatment for hyperthyroidism and thyroid cancer. We have studied these abnormalities for periods of up to fourteen years after I^{131} treatment of hyperthyroidism. Three groups of subjects were examined to date: 1. Controls: (a) 18 non-irradiated controls with no thyroid disease, 28-78 years of age; (b) thyrotoxic patients treated with surgery only, 24-46 years old. All controls showed abnormalities of count = 46 ± 2, 5% or less; ploidy 3% or less, achromatic lesions 2 or less, no chromosomal aberrations. 2. 54 treated hyperthyroids: (a) 42 treated 1950-1961 using 8-54 mc, aged 26-49 years; (b) 12 treated December 1962 to September 1963, using 8.3-12.7 mc, aged 27-61 years; blood was obtained before and 30 minutes after the dose. Seven of the 12 patients received antithyroid drugs before I^{131} therapy. 3. 9 thyroid carcinoma patients treated January-August 1963 in dosage of 150-200 mc I^{131} 16-49 years of age; blood was obtained before; 30 minutes and 2-48 hours after the therapy dose. The complete blood count of all cases studied was normal.

Conclusions: (1) an increased incidence of chromosomal abnormalities was found acutely and to a lesser extent chronically after I^{131} treatment of hyperthyroidism; (2) the incidence and severity of abnormalities was greater after the larger treatment dose used in treating thyroid cancer in the period shortly after treatment; (3) they persisted for the duration of follow-up (14 years) in hyperthyroid patients; (4) apparently no chromosomal abnormalities could be attributed to the use of antithyroid drugs.

S-12 *"Generalizations Derived From Radiobiological Experiments With Mammalian Cells In Vitro."* PAUL TODD, ROBERT TYM, JOHN T. LYMAN AND CORNELIUS A. TOBIAS, (Donner Laboratory, University of California, Berkeley, California.)

The radiation response of the colony-forming ability of a long-term line of human kidney cells (T1) has been studied under varying physical, chemical and physiological conditions. Specifically, the effects of linear energy transfer, anoxia, and potential radiation damage were investigated in combination.

Cultures irradiated with high-speed nuclei of D, He, Li, B, C, N, O, Ne, and A from the Berkeley HILAC show an increase of relative biological effectivness (RBE) up to a linear energy transfer (de/dx) of about 200 kev/μ above which value the RBE decreases with increasing dE/dx, but the inactivation cross-section appears to increase to a value somewhat greater than the size of the cell nucleus. The RBE is dose-dependent. Survival curves appear sigmoid in shape below dE/dx of 200 kev/μ and exponential at higher values of dE/dx; hence, sublethal damage and cellular recovery are reduced. Anoxic protection against X-rays is greater than two-fold and falls below 10 per cent at values of dE/dx greater than 150 kev/μ. No anoxic protection is observed above 300 kev/μ.

Cells bearing iodinated DNA are more sensitive to X-rays and to heavy-ion irradiation for dE/dx less than 200 kev/μ. These cells experience the same degree of anoxic protection as normal cells. Cells bearing sublethal damage acquired by pre-irradiation survive to X-irradiation in a manner similar to cells bearing halogenated DNA and are charcterized by altered growth and metabolism.

From the experimental data an empirical analytical expression for the dose response curves can be obtained and appears to be applicable to all conditions so far studied.

If the response of single cells is to be considered as a model for radiation therapy, these experiments suggest the desirability of pretreatment with iododenoxynucleosides, irradiation under aerobic conditions, dose fractionation, and the use of ionizing radiation of intermediate linear energy transfer, or, alternatively, simple exposure to beams of high dE/dx. The choice of conditions cannot be made independently of the nature of the response of the biological target and is contingent upon clinical applicability.

SATURDAY MORNING—JUNE 20, 1964

9:30 AM—WOMEN'S SCIENTIFIC PROGRAM

JOSEPH GREENBERG, CHAIRMAN

GRECIAN ROOM #2

Introduction—JOSEPH GREENBERG

Nuclear medicine is a fascinating specialty which has grown like Topsy since coming into its own shortly after the end of the Second World War. It already has done much in the fight against disease but we are just beginning to tap its potential. The Women's Scientific Program will outline what it is, how it works, what it costs and what its prospects are for the future.

How This Stuff Works—JOHN U. HIDALGO.

The solid foundation of nuclear medicine rests upon the instability of the nuclei of certain atoms. The instability of these atoms results in a change to a different kind of atom. When this change occurs, it is accompanied by the emission of certain radiations. All of the work in nuclear medicine depends upon the utilization of these emissions.

Diagnostic Use Of Radioisotopes—MILLARD N. CROLL.

After a warm-up review of current thyroid isotopic procedures, the "newer" radioisotope diagnostic studies will be discussed in two parts.

The first part will be the role of Iron-59 and Chromium-51 in evaluating blood dyscrasias and will include Ferro-chromo-kinetics and the use of organ localization of the isotopes by external counting techniques.

The second part will cover some of the more recent scintillation scanning procedures: spleen with BMHP, bone with strontium- 85, pancreas with Selenium-75, and lung with Iodinated serum albumin.

Therapeutic Uses of Radioisotopes—IRVING M. ARIEL.

Radioactive isotopes can be incorporated into any chemical and shaped to fit almost any physical method of therapy. The concentration of isotopes into a cancer or even the concentration of the radiation of radioisotopes into a cancer depends upon the ingenuity of the physician. There are some "well recognized" methods already in common use. For example, P^{32} for the treatment of leukemia or bone metastases from breast cancer. There are also intracavitary methods, intra-arterial and interstitial methods of applying radioisotopes. There are many examples of significant, though temporary, improvement of patients. There have even been some cures.

There Is A Teaching Problem Involved—SYLVIA FEDORUK.

At this Eleventh Annual Meeting of The Society of Nuclear Medicine, the charter members of the Society look back with great satisfaction at the many scientific discoveries and technological achievements in the field of Nuclear Medicine.

It is unfortunate, however, that although we have continuously struggled to carry out a satisfactory educational program on both the professional and non-professional levels, the results have been most unrewarding. Widespread misunderstanding of the many basic principles in the field of Nuclear Medicine still exists.

Somebody Has To Pay For It—EDMUND HALLEY.

In order to do the special kinds of diagnostic studies that are available with radioisotopes, and especially to do radioisotope therapy, a physician has to have more than the usual medical training. The "radioisotope" physician is a very special kind of a specialist. He must use complex and somewhat unusual equipment. Besides repair bills and maintenance costs, the physician invariably demands the help of highly trained assistants. The cost of the radioisotope itself might be very inexpensive but it can't be used as such. Radioisotopes used in humans are pharmaceutical and they must be prepared as such with even more care than is ordinarily given to drugs.

"THE FRIENDLY ATOM"—WALT DISNEY STUDIOS.

A ½ hour film on the peaceful uses of atomic energy.

SATURDAY AFTERNOON—JUNE 20, 1964

WORKS-IN-PROGRESS

SCANNING

Chairman, RAYMOND L. LIBBY

EMPIRE ROOM

W-1 *"Preliminary Evaluation of Color Scanning."* ROBERT T. MORRISON, TITUS C. EVANS (University of Iowa, Iowa City, Iowa)

With a recently developed commercially available color scanning attachment, more than 50 color scans have been made of the thyroid, the liver, the kidneys and the brain. Iodine-131, Mercury-203 and Gold-198 were utilized. Black on white dot scans and photoscans were made simultaneously with the color scan. On the basis of ease of recognition of abnormalities, the color scan was judged to be superior to the black on white dot scan and equal or superior to the photoscan. The color scan data is available for examination while the scan is proceeding and unlike the photoscan does not require chemical processing before examination. The quality of the color scan justifies the additional step in the adjustment of the scanner prior to starting the scan.

W-2 *"The Argonne Cancer Research Hospital's Brain Scanning System."* ROBERT N. BECK, DONALD B. CHARLESTON, PAUL EIDELBERG and PAUL V. HARPER (The University of Chicago, Chicago, Illinois.)

The use of conventional, general purpose, radioisotopes scanning systems for detecting brain lesions is limited by the time required. The research scanner described here was designed to study techniques for minimizing this period without increasing the radiation dosage to the patient or sacrificing spatal resolution or statistical reliability.

The system consists of four scintillation detectors arranged in opposing pairs, which scan both sides of the patient's head simultaneously. These detectors are housed in lead shields which accept interchangeable focused collimators designed to give maximum counting efficiency for specific gamma energies. Detected gamma pulses are fed to a transistorized electronics unit consisting of four pulse height analyzers, together with pulse forming circuits for photographic recording on two sheets of film, one for each side of the patient's head. Photopeak gamma pulses from each channel produce bell-shaped spots on film by means of pulsed light projectors.

For each channel a calibration step wedge is produced on the film record by a random pulse generator which produces count rates of 100 to 9500 counts per minutes in twenty-six steps of 20% increase. This permits a quantitative measure of the count rate at any point on the patient's head.

Small lights in the center holes of collimators on one side are focused on photodiodes in the opposite collimators. Signals produced by this system outline the patient's head on the film record and reverse the scan direction to minimize the time spent in scanning beyond the head.

A dual channel optical sytsem records data relating to the scan (patient's name, isotope injected, scan speed, etc.) on each film record, together with an appropriate LEFT or RIGHT mark for unambiguous identification of the film.

Using Tc^{99m}, and a scan speed of 2.5cm/sec., this system produces pictures of conventional quality of both sides of the patient's head in 90 seconds. If the scan time is extended to 15 minutes, the scan pictures are decidedly improved.

W-3 *"Quantitation of Dynamic Processes with the Digital Autofluroscope."* MERRILL A. BENDER and MONTE BLAU (Roswell Park Memorial Institute, Buffalo, New York.)

The detector of the new digital autofluoroscope consists of 260, 2 inch thick, 3/8 inch diameter NaI (T^1) crystals packed in 20 files and 13 ranks in a 6 × 9 inch array. Each of the 260 crystals is optically coupled to two plexiglas light pipes with the 20 light pipes from a given rank going to one phototube and the 13 light pipes from a given file going to another phototube. A pair of pulses occurring simultaneously in a rank phototube and a file phototube uniquely identifies the crystal in which the interaction occurred. The position signal derived from the phototube array is independent of pulse height. Anticoincidence circuits reject those simultaneous pulses arising from a Compton interaction followed by the absorption of the scattered radiation in an adjacent crystal. The advantages of this system of data transfer will be documented by the presentation of efficiency and intercrystal crossover data.

The digital nature of the light pipe system permits the use of magnetic core storage with subsequent non-destructive continuous readout on a full size CRT and numerical printout for quantitative analysis.

W-4 *"Diagnostic uses of the Scintillation Camera."* A. GOTTSCHALK and H. O. ANGER (University of California, Berkeley, California.)

The 11-1/2 inch diameter crystal now used in the scintillation camera provides a large enough field of view to image organs normally scanned in humans.

Renal scintiphotos are obtained with 5-minute exposures after intravenous injection of 50 μc of Hg^{203} Neohydrin. However, in a nine year old child when dose reduction was desired, excellent pictures were obtained with 5 μc of Hg^{203} and a 15 minute exposure. In about 90% of adult patients, both kidneys are visualized in a single picture.

Renal dynamics have been investigated by taking time lapse movies following injection of 150-250μc of I^{131} Hippuran.

Multiposition (supine, prone) hepatic imaging is easily accomplished because exposures can be made in 5 minutes with a dose of 100μc of I^{131} Rose Bengal. The examination is completed in 1/2 hour or less, before significant filling of the gall bladder or duodenum has occurred.

The 10-fold reduction in examination time with the scintillation camera compared to scanners will be illustrated by brain scintiphotos taken after conventional doses of Hg^{203} Neohydrin and Tc^{99m}.

W-5 *"Scanning the Brain in Cross-Section."* DAVID E. KUHL (School of Medicine, University of Pennsylvania Hospital, Philadelphia, Pennsylvania.)

With this method, a pair of detectors makes a sequence of tangential scans at regular angular intervals of 15° around the level of the brain under study. In a scanning time of approximately 10 minutes, the counting and positional data representing the radioactivity of each thin cross-section of the brain is recorded on perforated paper tape. These data are then regenerated with time compression to display the section image on the film of an oscilloscope camera in approximately 10 seconds.

The added dimension of depth inherent in a transverse section image has already given us clinical information about the distribution of some brain tumors that was otherwise unavailable. The present direction of our investigations will be discussed in view of the potential of transverse section brain scanning.

Cases with mitral stenosis, valvular, hypertensive, and congenital heart disease, with and without decompensation, were examined. Changes in regional blood flow were compared taking the flow rate per unit volume of right lower lung as 100%. In normals the upper lobe has less flow than the middle or lower lobes both in standing and recumbent position. In compensated mitral stenosis the upper lobe has 50% more flow than the lower lobe. In congestive heart failure with or without valvular disease the upper lobe also shows an increase in flow (200% to 400% of right lower lobe) and returns to normal when decompensation is corrected.

SATURDAY AFTERNOON—JUNE 20, 1964

WORKS-IN-PROGRESS NEWER METHODS SESSION

Chairman, RICHARD E. PETERSON

GOLD ROOM

W-6 *"Regional Pulmonary Blood Flow in Cardiac and Pulmonary Disorders."* HIDEO UEDA, MASAHIRO IIO and SHIGEKOTO KAIHARA (University of Tokyo, Tokyo, Japan.)

Quantitative information of pulmonary blood flow can be obtained if a digital dot scan is performed after intravenous injection of macroaggregated albumin (particle size more than 50 μ) labeled with I-131 or Cr-51. The regional distribution of the aggregated albumin in the organ represents the segmental blood flow provided complete mixing occurs before distribution of the material. All the particles are in the capillaries during the first circulation and no significant metabolism occurs during the time of observation.

For the digital evaluation, rapid whole chest scanning (properly selected rates without cutoff) has been performed followed by the regular scan of the lung. The former was used for the quantitative analysis of the blood flow in the selected lung fields which are determined by the latter scan (and X-ray).

W-7 *"Counting Characteristics of a Medium-Level Whole-Body Counter."* HIROTAKE KAKEHI, R. L. HAYES, (Japan and Oak Ridge)

Preliminary to clinical use, basic measurements are being made on a medium-level whole-body counter (ORINS). This counter will be used to bridge the sensitivity gap between high-level and low-level counters and will be most useful for clinical diagnosis of the patients having activity retentions of 0.1 to 100 microcuries.

Initial measurements have been made of background counting rate, linearity between counting rate and radioactivity, and isoresponse patterns on the stretcher to be used by the patients.

At present, using compartmentalized phantoms, the spectra of various radioisotopes are being studied to determine how they vary with the location of the sources. Spectra of point and diffusely distributed sources at the top, center and bottom of the phantoms have been compared with each other.

It is anticipated that this study will provide a method for estimating accurately the amount of radioactivity in a human body independent of the distribution of the radioactivity.

W-8 *"Preoperative Localization of Parathyroid Adenomata."* JOSEPH B. WORKMAN and THOMAS B. CONNOR (University of Maryland, Baltimore, Maryland)

Since November 1960 eight patients with hyperfunctioning parathyroid adenomata have been studied in a search for a satisfactory method of pre-operative localization.

The major effort has been directed toward increasing the concentration of radio-cobalt labeled Vitamin B-12 in parathyroid tissue. The general study plan includes the following:

A) Pre-operative scintillation scanning using standard medical scanning equipment.

B) Tumor identification at the time of surgery, using a small surgical scintillation probe.
C) The relative concentration of isotope per 100 mgm tissue obtained at the time of surgery from tumor, thyroid gland and skeletal muscle.

Size is probably the most important of the many variables effecting successful tumor identification for the relatively small size of the adenomata encountered in this series appears to have hampered localization. Positive identification of hyperfunctioning parathyroid adenomata at the time of surgery was possible in 3 patients using a small crystal scintillation probe. Concentrations of isotope per 100 mgm of parathyroid tissue exceeded that of other tissues by at least a 4:1 ratio in all eight patients.

W-9 *"Localization of I°HSA in Rheumatoid Joints."* WILLIAM S. MAXFIELD, THOMAS E. WEISS, PAUL J. MURISON and JOHN U. HIDALGO (Ochsner Clinic, New Orleans, Louisiana)

Tracer studies with I°HSA in patients with normal joints demonstrate that following the I.V. injection there is a transient rise in activity in the wrist and knee joints. At 24-hours the count rate has returned to the 1-hour level or below. In the rheumatoid patient the initial localization of I°HSA in involved wrist and knee joints is greater than the localization found in the normal patient. The increased localization in the rheumatoid patient is maintained at 24-hours. This increased localization can be demonstrated by scanning as well as external counting. Preliminary investigation suggests that the I°HSA localization may be an objective method of measuring the state of the disease as the intensity of localization seems to parellel the clinical assessment of the degree of rheumatoid activity. The test may prove to be very sensitive as higher than normal localization of the I°HSA has been found in clinically quiescent joints.

W-10 *"Continuous Regional Blood Flow Measurements by Inhalation of Radioactive Xenon."* ALBERT E. JOHNSON and FRANK GOLLAN (VA Hospital, Coral Gables, Florida)

The purpose of the present study is to evaluate the inhalation of radioactive xenon and then the continuous external monitoring of its washout as a measurement of regional blood flow. The assumptions of constant equilibrium between tissue and venous xenon concentration; the wide range of solubility and partition coefficient in various tissues, and homogeneity of capillary flow, made a controlled study desirable.

Anesthetized dogs inhaled radioactive xenon until equilibration in a leg muscle was reached. Then the animal was killed by an intracardiac potassium injection and the isolated leg was perfused with a pump-oxygenator via the external iliac artery. The venous blood from the iliac vein was drained into a bubble oxygenator which removed the xenon and thus prevented recirculation. Blood flow was measured with an electromagnetic flowmeter. Changes in blood flow from 0 to 220 cc/min. were recorded simultaneously with xenon clearance rates and direct flow measurements. The analysis of the data showed that the xenon clearance did correlate with the blood flow delivered by the pump within 15%.

Such measurements can probably still be improved if each flow rate is measured separately during the first 12 minutes of desaturation when the curve is steeper. Failure to detect changes of xenon clearance rate from the muscle of the hind leg of intact dogs after intravenous administration of levarterenol or breathing of increased carbon dioxide concentrations is probably due to large collateral arteriovenous shunts preventing the washout of xenon from muscle tissue.

SATURDAY AFTERNOON—JUNE 20, 1964

WORKS-IN-PROGRESS

TRANSPORT KINETICS

Chairman, MILLARD CROLL

EMPIRE ROOM

W-11 ***"Iron Absorption in Iron Storage Diseases."*** **H. S. WILLIAMS, R. S. WILLIAMS and C. S. PITCHER (The Royal Free Hospital, London, England)**

Iron absorption has been studied using the double isotope technique. ^{55}Fe as ferric chloride was given in water in the course of a standard meal and ^{59}Fe given intravenously as labeled plasma. The iron in blood taken two weeks later was electroplated on to copper discs and the ^{59}Fe and ^{55}Fe assayed using a Geiger counter and a beryllium-window proportional counter.

The mean value of iron absorption in 40 normal subjects was 7.5%.

Sixteen patients with haemochromatosis were studied—some before venesection therapy, some during treatment and the rest one year after completion of treatment. Markedly increased absorption was found during venesection therapy and in a number of patients studied a year later.

Six out of 12 relatives of patients with haemochromatosis had definitely increased absorption of iron and 3 others had absorption at the upper limit of the normal range.

Finally, absorption rates are presented for a group of 42 patients with cirrhosis. The significance of the increased absorption found in 18 of the 42 patients is discussed in relation to the pathogenesis of haemochromatosis.

W-12. ***"Unusual Iron Deposition in Idiopathic Pulmonary Hemosiderosis and Paroxysmal Nocturnal Hemoglobinuria Studied by Fe^{59} Kinetics."*** **M. POLLYCOVE, M. FISH and J. H. LAWRENCE (University of California, Berkeley, California)**

In most pathologic conditions in which Fe^{59} kinetic studies are performed, sufficiently complete information is obtained from external monitoring over only such hematologically important organs as the liver, spleen, or bone marrow. However, unusual conditions exist in which there is abnormal deposition of iron in organs other than those mentioned, and where external monitoring of the involved organs provides critical information in the analysis of the disease process. Two of these unusual conditions are Idiopathic Pulmonary Hemosiderosis, in which pulmonary deposition of iron occurs, and Paroxysmal Nocturnal Hemoglobinuria, in which renal deposition of iron is prominent.

We have studied 4 cases of IPH with Fe^{59} kinetics. The prominent findings were related to repeated episodic hemorrhage into the lungs. This resulted in a red cell kinetic pattern similar to that commonly seen with episodic hemorrhage and blood loss from the body in gastrointestinal bleeding, menorrhagia, etc. In two cases the degree of hemorrhage and irreversible iron loss into the lungs was sufficient to produce iron deficiency anemia. External monitoring and total body scanning clearly showed the accumulation and persistence of Fe^{59} in the lungs following the hemorrhage of radioactive erythrocytes into this organ.

Four patients with PNH were studied. External monitoring showed a gradual but marked accumulation of Fe^{59} in the kidneys achieving a constant maximum, i.e., an equilibrium after 2½ weeks. In one patient given daily intravenous infusions of dextran, a repeat from kinetic study demonstrated no accumulation of radioiron in the kidneys; daily body loss as measured with a whole body counter was simultaneously shown to be arrested. In two cases the loss of iron from the body through the kidneys was sufficiently severe to result in iron

deficiency anemia. The pattern of renal accumulation of Fe^{59}, combined with the iron kinetic analysis, is sufficiently unique to make it pathognomonic for PNH.

The results of iron kinetics studies in these two conditions establish the value of additional monitoring, total body scanning, and the whole body counter as adjuncts to iron kinetics studies in the demonstration of unusual pathways of iron movement.

W-13 *"The Role of Gastrointestinal Mucousa in Iron Excretion."* Richard E. Peterson and Robert F. Cech (State University of Iowa, Iowa City, Iowa)

Crosby has suggested that the glandular epithelium in the stomach and duodenum serve as an additional control mechanism in unloading iron above body requirements. To examine the clinical evidence for this, all feces were collected for 10 to 14 days after administering Fe^{59}. In four patients given oral doses of 0.5 μc, the daily samples revealed a secondary rise in fecal Fe^{59} consistent with the desquamation of Fe^{59} labeled mucousa into the fecal stream. This "peak" was noted 8, 9, 11 and 12 days after the dose was administered. Four other patients were similarly studied after intravenous doses of 5.0 μc of Fe^{59}. In these individuals the secondary rise occurred on 8, 8-10, 10 and 12 days after the date of the dose. In six non-anemic individuals, this secondary rise ranged from 215 to 311 per cent of the average fecal Fe^{59} excreted between the 6th and 14th days after dose. A patient with Iron Overload Syndrome had a secondary rise equivalent to 540% and a patient with iron deficiency showed no secondary rise on one occasion and on repetition a small secondary rise of 140% was noted.

W-14 *"Liver and Spleen Scanning with I^{131} Colloidal Albumin."* Merle K. Loken, Edward V. Staab and Andrew Shea (University of Minnesota Hospitals, Minneapolis, Minnesota)

I^{131} colloidal albumin is presently being used for liver and spleen scans. A comparison of these scans is being made to those obtained using colloidal gold-198, I^{131} Rose Bengal and heat treated erythrocytes tagged with Cr^{51}.

We find that the I^{131} colloidal albumin is taken up by the liver very rapidly after intravenous administration. Its clearance half-time from the liver is approximately one hour. The liver clearance does vary somewhat from patient to patient and possible reasons for this are being investigated. Because of the rather rapid liver clearance, the scan is normally started within 10 minutes after the administration of 2-4 microcuries of I^{131} albumin colloid per kilogram. By doing so we obtain acceptable liver scans in most patients although the later portions of the liver scan tend to be less well visualized than does the early part of the scan. In addition, we find that the uptake pattern of I^{131} colloidal albumin tends to be more irregular than that seen with either colloidal gold-198 or I^{131} Rose Bengal.

The per gram uptake of colloidal albumin in the spleen is usually greater than in the liver and its clearance is less rapid than observed for liver. Thus, the timing of the scan after isotope administration is less critical and the spleen scans tend to be more satisfactory.

W-15 *"Cardiac Output by Surface Counting by An Automatic Method."* Philip C. Johnson, Jr. and Charles E. McCullough (Baylor University College of Medicine, Houston, Texas)

The radioactive method for measuring cardiac output with a detector placed on the chest wall has been shown by several groups to give values for cardiac output which correlate closely with non-radioactive methods. The radioactive method has the advantage of not requiring arterial sampling and/or cardiac catheterization. Others have been unable to obtain a satisfactory correlation between the radioisotope method and standard methods. Their criticism has generally revolved around the lack of statistical accuracy of the curves. For an accurate result, surface counting method requires optimization between the count rate and integration constants, careful extrapolation of the exponential downslope through re-

circulation and accurate calculation of area by planimeter. Slight mistakes in this extrapolation or area calculation can produce significant errors in the cardiac output values obtained. To avoid the pitfalls of hand extrapolations we have developed an integrator-computor which automatically calculates cardiac output directly from the output of the rate-meter or tape recorder thus avoiding the errors and bias of planimetered areas and extrapolations estimated by eye. Comparison of the cardiac output values determined by the machine with simultaneous Fick and arterial dilution curves shows close correlation between the values obtained in dogs and man, including high and low cardiac outputs.

SATURDAY AFTERNOON—JUNE 20, 1964

WORKS IN PROGRESS

BRAIN

Chairman, NORMAN J. HOLTER

GOLD ROOM

W-16. ***"Isotopic Localization of Cranionasal Cerebrospinal Fluid Leaks."*** **GIOVANNI DI CHIRO and PATRICK M. REAMES (Dept. of HEW, Bethesda, Maryland)**

While the diagnosis of cerebrospinal fluid rhinorrhea is generally quite simple, the assessment of the leak site may be very challenging. This is due to the fact that meningeal breaks may occur in various locations. A pneumoencephalographic localization of such a leak has not been reported though in a few instances such a diagnosis has been made using the contrast medium, Pantopaque. An innocuous and reliable method of localizing such leaks would represent a significant advance considering that even at operation it is difficult to recognize where the meninges are disrupted and that successful surgery can only be carried out if the exact leak place is recognized. Such a diagnosis of the leakage site has been made by us in several cases by scanning of the head after lumbar injection of 100 microcuries of I*HSA (I*HSA-Cisternography). The one and two hours scans after the intrathecal introduction of the isotope are the most useful.

W-17 ***"The Detection and Localization of Cerebrospinal Fluid Fistulae."*** **JOYCE C. KLINE, FLAVIO PULETTI, MAXINE BENNETT and JOHN R. CAMERON (University Hospitals, Madison, Wisconsin)**

The detection and precise localization of cerebrospinal fluid fistulae are essential for adequate surgical management. A simple technique using Na^{24} injected into the cysterna magna and detected on cotton pledgets placed near the ostea of the paranasal sinuses and eustachian tubes. $Sodium^{24}$ diluted in the CSF enters the blood stream rapidly, raising the radioactivity level on the pledgets contaminated with blood from minor hemorrhages due to the placement procedure. This has led to difficulty in interpretation of the final results in several patients The larger molecular size of I^{131}-tagged human serum albumin (I*HSA) prevents its rapid entrance into the blood from the CSF and avoids this difficulty.

Cotton pledgets, coded to location by knots in their attached threads, are placed at the ostia of the paranasal sinuses and Eustachian tubes. One hundred microcuries of I*HSA are injected into the cysterna magna. The patient's head is then lowered and moved about to insure diffusion of the I*HSA in the CSF. He then remains sitting for one to two hours, after which the pledgets are removed, placed in test tubes, and their activity determined in a

well counter. Pledgets from the involved area show a level of radioactivity twenty to one hundred times above that of uninvolved areas. The rise in blood radioactivity during the observation period is too small to interfere with interpretation.

W-18 *"Velocity/Time Relationships in the Cerebral Circulation."* ROBERT L. BELL (VA Center, Wadsworth, Kansas)

By measuring velocity of an arterial radioactive bolus at certain convenient sites, it is possible to describe a velocity/time relationship for the cerebral circulation. The measurements are obtained at the carotid input, jugular output, and over the sagittal sinus. Normal cerebral circulation has a uniform linear velocity-time relationship with a gradient decreasing from artery to vein. However, with addition of tumor or abscess or subdural hemorrhage, there is a distortion of this basic pattern so that the measurements deviate from the normal velocity/time relationships and become irregular. This data can be evaluated and correlated with serial arteriograms.

W-19 *"Measurement of Brain Circulation Time by an Intravenous Radioisotope Technique."* W. H. OLDENDORF and M. KITANO (V.A. Center, Los Angeles, California)

50 microcuries of labeled hippurate is deposited rapidly into the right heart after injection into an anticubital vein, after obtaining venous congestion and total stasis in the arm. Stasis is suddenly released and the bolus passes through the cardiopulmonary circulation. A portion of the material leaving the heart passes through the brain. Since hippurate is relatively non-diffusable in brain it passes on through. The total cranial content is monitored externally and the count rate builds up and falls off as a function of the passage of the isotope.

A reference point for the bolus entering and leaving the brain is established by noting the entrance and exit from the brain blood pool of the most concentrated part of the bolus. The entrance and exit results in a maximum rate of increase and decrease of the brain isotope content and is displayed by directly plotting the first derivative of the count rate obtained from the head. This establishes the most common circulation time through the brain. Each test is recorded on magnetic tape.

Over 500 such studies have been performed, including normals and a variety of pathology. Normal ranges will be discussed. The circulation time seems to be lengthened in the presence of polycythemia, clinically recognized cerebrovascular diesase, and certain brain metabolic diseases. It is lengthened by hyperventilation and shortened by CO_2 inhalation. Arteriovenous malformations cause a shortening. Characteristic curves in normals and abnormals will be presented along with a brief motion picture demonstrating the application of the technique.

W-20 *"Use of I^{131} Iodipamide for Brain Tumor Detection."* ROBERT A. NORDYKE and H. WILLIAM GOEBERT, JR. (Straub Clinic, Honolulu, Hawaii)

Labeled substances currently used in conjunction with mechanical photoscanners for brain tumor localization have certain disadvantages: Hg^{203} chlormerodrin gives unnecessarily high kidney radiation; Hg^{197} chlormerodrin has a half-life which is too short for practical use at reasonable cost; I^{131} serum albumin subjects the patient to a relatively high total body radiation and provides a poor tumor-background ratio.

I^{131} iodipamide (Cholografin) has certain qualities which make it theoretically preferable to the other materials. It is carried in the blood by albumin and is nonspecifically picked up by brain tumors. In addition it has the qualities of a longer physical half-life, a relatively rapid excretion via the liver, increased target-nontarget ratio and reduced total body and specific organ radiation.

In a series of patients with suspected brain tumors or other intracranial lesions, we are currently comparing several detection methods: electroencephalography, pneumoencephalography, aortography, Hg^{197} chlormerodrin photoscanning and I^{131} iodipamide photoscanning.

SATURDAY AFTERNOON—JUNE 20, 1964

WORKS-IN-PROGRESS

METABOLIC BEHAVIOR

Chairman, LINDON SEED

EMPIRE ROOM

W-21 *"Radiobiological Differences Between I^{131} and I^{125} in the Mouse."* WILLIAM J. SCHINDLER and ROBERT A. LIEBELT (Baylor University College of Medicine, Houston, Texas)

Single injections of 2, 5, 20, 50 or 200 μc I^{131} or I^{125} were given to 674 Swiss mice (both sexes) and radiobiological effects on the thyroid were studied from 1 day to 9 months following the injections. Histological studies showed that 200 μc I^{131} resulted in total destruction of thyroid gland within 7 days with earliest signs of cellular damage noted at 3 days. 50μc I^{131} caused partial thyroidal destruction by 14 days. 200 μc I^{125} caused only minor morphological changes (during comparable periods) which were reversible. Mice given 200 μc I^{131} showed the following physiological defects at the times indicated after injection: a) 48 hours.—*in vivo* release of radioactivity from the gland markedly accelerated and slope of release curve acutely changed indicating "pouring out" of glandular contents due to damage. b) 6 days—inability of the thyroid gland to respond to TSH. c) 8 days—activity of the thyroidal "iodide pump" completely absent (T/S ratio 0). d) 3 mo. and 7 mo.—majority of animals showed no thyroidal uptake, however 2 animals did take up some iodine but could not retain it. All other animals showed normal thyroidal activity by these criteria of release curves, response to TSH, T/S ratios and thyroidal uptake. T/S ratios were done using Tapazole® to block organic binding and then, one hour before killing, the other radioisotope was injected to measure inorganic iodide in the thyroid and serum (I^{131} and I^{125} were countered simultaneously using gamma ray spectrometry and a well-type scintillation counter). Much of the energy of I^{125} (conversion and Auger electrons) would be absorbed very close to their point of origin; therefore may be treated as "β-like radiations" for dosimetry. In spite of this, I^{125} produces less thyroidal radiation damage than I^{131}.

W-22 *"In Vivo Mobilization of Barium-137m."* R. L. HAYES and J. E. CARLTON (Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee)

Cesium-137 ($T_{1/2}$= 30 y) decays by pure beta emission to Ba^{137m} ($T_{1/2}$= 2.6 min), which in turn decays mainly by gamma emission to stable Ba^{137}. Daughter Ba^{137m} is distributed in the rat in a pattern different from that of parent Cs^{137}, even though the half-life of Ba^{137m} is quite short. Conceivably, the excess of Ba^{137m} in blood might be used as a diagnostic test of the rate of blood flow and of general metabolic rate. Its determination in the blood would be a measure of the mobilization rate of Ba^{137m} from muscle tissue, which in turn might be governed mainly by the rate of blood circulation through muscle tissue, although other factors such as cell permeability, lymph flow, etc. could be of importance as well.

Studies with rats have shown that the Ba^{137m} to Cs^{137} ratio of blood taken from the aorta rises with time after intravenous administration of Cs^{137}. This is apparently caused by a more rapid drop-off of Cs^{137} activity in the vascular compartment as compared to that in the extravascular compartments. On the other hand, the percentage of extravascular Ba^{137m} mobilized into the vascular compartment was found to be constant. States of anesthesia, hypothermia, and hyperthermia in the rat have produced significant differences in the percentage of Ba^{137m} mobilized.

W-23 *"Calcium-45 Metabolism and Osteoporosis in the Dystrophic Mouse."* JOSEPH L. RABINOWITZ, CAROL ANN WELSH and CONNIE R. CECALAS, (VA Hospital, Philadelphia, Pennsylvania)

By the use of 1 microcurie of Calcium-45 chloride injected intraperitoneally, 72 hours prior to sacrifice into dystrophic mice and their littermates, osteoporosis of the long bones of the dystrophic mice was readily confirmed by autoradiography and microroentgenology. During this work it was observed that mock surgical trauma changed the uptake of Calcium-45 in various tissues. This work also indicated the existence of differences in Calcium-45 uptake of the various tissues of the dystrophic mice as compared to the tissues of the littermates. It was observed also that the salivary glands (parotid) of mice showed the largest calcium uptake of any of the tissues studied. We are presently attempting to determine by ultracentrifugation the ratio of plasma calcium in its protein-bound and protein-free fractions in both the dystrophic mice and their littermates.

W-24 *"An Approach to the Detection of Occult Pigmented Melanoma."* M. S. BLOIS, JR. (Stanford University School of Medicine, Palo Alto, California)

Pigmented melanoma tissue differs from other normal or abnormal tissues in one unique respect: its relatively high rate of melanin synthesis. Many tissues including the choroid of the eye, the substantia nigra, and probably the pineal body, appear to synthesize this pigment at a low rate. The skin synthesizes melanin at a somewhat higher rate in order to compensate for the loss of pigment by exfoliation.

Using C-14 labeled dihydroxphenylalanine (DOPA), a precursor of melanin (and epinephrine) synthesis, the distribution in the various tissues of mice with transplanted melanomas, has been studied. The distribution of radioactivity in mice with the Harding Passey melanoma has been found to be similar to that reported by Hempel and Deimel but for a spontaneous mouse melanoma and which is more highly pigmented, the tumor uptake is very pronounced. The specific activity of this tumor following a single dose of C-14 DOPA is found to be from 10 to 100 times the activity in the spleen or liver. Our interpretation is that the selectivity of uptake of the precursor into the pigment is proportional to the rate of pigment synthesis.

In order to use this approach for the detection and localization of pigmented melanomas and their metastases, by scanning, it is necessary to have a gamma emitting isotope which is incorporated into a suitable melanin precursor.

W-25 *"Degradation of C^{14}-Labeled Thymidine and Its Halogenated Analogs in Man."* JOSEPH P. KRISS, RICHARD K. SHAW and NIKKI EDMUNDS (Stanford University, School of Medicine, Palo Alta, California)

The rate and extent of degradation of 2-C^{14}-thymidine (TdR), 2-C^{14}-bromodeoxy-uridine (BUdR), and 2-C^{14}-iododeoxyuridine (IUdR) have been compared in 11 adult patients after the intravenous administration of 10-20 μc doses of each compound, utilizing an apparatus which continuously monitors and records CO_2 content and C^{14} activity in the expired breath. Measurements were made for a period of 60-90 minutes after injection of the labeled compound. The output data from the detectors was analyzed manually and was also programmed for computer analysis. The curve of decline in $C^{14}O_2/C^{12}O_2$ specific activity with time could be reserved into 2 exponentials, the slower of which had a mean T ½ of 84 minutes for TdR and about 60 minutes for BUdR and IUdR, probably representing the degradation rates of the breakdown products thymine and uracil, respectively.

During the first hour after injection, the mean percentage C^{14} recoveries in the breath were 40, 38, and 46 for TdR, BUdR, and IUdR, respectively. The total mean C^{14} recoveries, usually complete within 8 hours, were calculated to be 92, 66, and 94 per cent, respectively. In every patient, the total recovery of C^{14} after injection of C^{14}-BUdR was lower than that

after TdR or IUdR administration. The urinary excretion of C^{14} was low after injection of each of the labeled compounds, averaging about 2% of the administered dose, with a range of 0.1-5.3%. The calculated mean net bodily retention of TdR, BUdR, and IUdR under these non-loading conditions was, therefore, about 6, 32 and 4 per cent, respectively. Preliminary observations indicates that bodily retention of these compounds may be significantly increased in patients with myeloproliferative diseases. These results have important implications for the systemic use of the halogenated thymidine analogs as antivirus agents or as radiosensitizers.

W-26 *"Differential Diagnosis of the Megaloblastic Anemias Using C^{14} Histidine, C^{14} Proprionate and $C^{14}O_2$ Breath Analyses."* M. FISH, M. POLLYCOVE and T. V. FEICHTMEIR (University of California, Berkeley, California)

Folic acid deficiency results in the inability to transfer the 2 (ring) carbon atom of histidine to the one carbon pool where it would either be oxidized to CO_2, or incorporated into nucleoprotein, or other relatively fixed body constituents. Likewise, vitamin B_{12} deficiency results in the inability to convert proprionate into succinyl-CoA. When the 2-carbon atom of proprionate is incorporated into succinyl-CoA, it subsequently is either oxidized to CO_2, or incorporated into heme or other relatively fixed body constituents. Thus, theoretically, patients with folic acid deficiency should have impaired ability to form $C^{14}O_2$ when given histidine-2(ring)C^{14} and patients with vitamin B_{12} deficiency should have impaired ability to form $C^{14}O_2$ when given proprionate-2 C14. We have found this to provide a rapid accurate way to differentiate the megaloblastic anemias due to either folic acid deficiency or vitamin B^{12} deficiency.

When 25 microcuries per 0.5 mg of C^{14}-histidine was given intravenously to two normal subjects and 19 subjects with megaloblastic anemia, and the pattern of $C^{14}O_2$ production was studied with the $C^{14}O_2$ breath analyzer, the following results were obtained for the cumulative C^{14} excreted in the breath during the first 60 min. (expressed as per cent of injected dose): two normal subjects 1.12 and 1.18%; eleven vitamin B_{12} deficient subjects 0.48-1.71%; eight folic acid deficient subjects 0.06-0.35%. In addition, six patients who previously had megaloblastic anemias of either etiology, but who were in remission under specific therapy at the time of the study, had a cumulative excretion of 0.79-1.34% in twenty minutes. Thus, this test clearly differentiated patients with folic acid deficiency from normal subjects, vitamin B_{12} deficient subjects, or patients with megaloblastic anemia in remission under specific therapy.

Similarly, the administration of 25 microcuries per 0.25 mg of proprionate-$2C^{14}$ to vitamin B_{12} deficient patients resulted in a pattern of $C^{14}O_2$ excretion clearly distinguishable from the normal.

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WORK-IN-PROGRESS

NEWER MATERIALS

Chairman, JOHN U. HIDALGO

GOLD ROOM

W-27 *"The Metabolism of I^{131}-Insulin in Patients with Diabetes Mellitus."* SHIGERU TANAKA and KEMPO TSUKAMOTO (Japan)

0.8 μc of I^{131}-insulin per kg body weight was injected intravenously in 15 diabetic patients treated with insulin, in 15 patients without insulin and in 10 non-diabetic controls.

Four scintillation detectors were placed on the regions of heart, liver, muscles (lower limb), and urinary bladder, and activities recorded continuously for 30 minutes. In some patients a profile-scanning was done at ½, 2, 4 and 24 hours. Heparinized whole blood was withdrawn at 5, 30, 60, 120 minutes, and 24 hours. The disappearance of I^{131}-insulin in the plasma was determined by counting the TCA precipitate in a well type scintillation counter.

The radioactivities recorded from the regions of heart and muscles showed a temporary decrease followed by a gradual increase, even though the amount of I^{131}-insulin in the blood plasma was steadily decreasing. The curve obtained from the region of liver had a similar pattern to a radioisotope renogram, indicating that I^{131}-insulin was taken up by the cells of liver and then excreted or degraded. In the profile-scanning, the majority of I^{131} was located in an area of liver at 30 minutes. At 2 hours, approximately one-half of I^{131} was shifted to the region of the urinary bladder.

The diabetic patients with insulin treatment had less radioactivity in the area of liver and muscles than diabetic patients without insulin and non-diabetic controls. The disappearance of I^{131}-insulin from the blood plasma was much slower and the excretion of I^{131} in the urine was much lower in diabetic patients treated with insulin. It was also found that much more I^{131}-insulin was bound to plasma protein in these patients by means of a sephadex column.

W-28 *"Relative Incorporation of Antimony from Tartar Emetic and Astiban by* Schistosoma Mansoni *and* Schistosoma Haematobium." A. SCHULERT, E. McCONNELL, H. BROWNE and Z. FARID (Nashville, Tennessee and Cairo, Egypt)

Through the use of tartar emetic (potassium antimony tartrate) and astiban (sodium, antimony, 2, 3-meso-dimercapto-succinate) labeled with antimony-124, the uptake of antimony by Schistosome worms and ova is readily determined. When astiban is given to a hamster infected with *Schistosoma mansoni* the uptake in male worms is about one-third that of liver, female worms about equal to liver, but the uptake in the Schistosome ova is ten times that of the female worms.

The comparative fate of antimony from tartar emetic and astiban were compared in hamsters infected with *S. mansoni* and others infected with *S. haematobium*. In addition, the comparative antimony uptake of *S. haematobium* ova excreted in the urine of patients treated with tartar emetic and astiban was determined. Both male and female *S. mansoni* worms take up about 70 per cent more antimony from tartar emetic than from astiban. The relative antimony uptake by *S. haematobium* ova which are collected in the excreted urine of man is more than ten times greater with tartar emetic than with astiban.

The findings suggest that tartar emetic is the more effective drug, although astiban has the advantage of intramuscular administration whereas tartar emetic must be given intravenously.

W-29 *"Turnover of Tritiated Water in Mycobacteria (B.C.G.)."* JOSEPH STERNBERG and ARMAND MERCIER (University of Montreal, Montreal, Canada)

Tritiated water was added to a Sauton medium in a concentration of 40 microcuries per ml; the medium was inoculated with B.C.G. and the distribution of tritium was determined in the cells harvested at 21 days after inoculation.

The T_2O constituted a label for 94.2% of the hydrogen in the culture medium, the remaining 5.8% originated from glycerin and to a far lesser extent from asparagin.

In the microbial cells, the specific activities of the lipids far exceeded that of the water-soluble components and insoluble cell residues (respectively 0.735, 0.107 and 0.220).

The analysis of the microbial constituents shows that water has a significant role in the pathway of lipidic elaboration since close to 75% of the H atoms are provided by H or OH; on the other hand, only 10% of the residues originate from water.

This result suggests that lipidic synthesis in microbe involves the same exchange with water as that in animal tissues, at least in the metabolic pathway of cholesterol.

W-30 *"Radioalbumin Macro-Aggregates for Lung Scanning."* G. V. TAPLIN, M. L. GRISWOLD, D. E. JOHNSON, H. S. KAPLAN and M. M. AKCAY (University of California, School of Medicine, Los Angeles, California)

Human lungs may be scanned immediately after intravenous injection of 100-200 μc of 5-25 μ size radioalbumin aggregates because they are temporarily trapped in the lung capillaries ($T_{1/2}$ = 1-2 hours). Apparently these fragile clusters of loosely bound fine particles become fragmented in the lung capillaries and return to the general circulation. Then with each subsequent passage of blood through the liver-spleen the small particles are extracted with high efficiency, mainly by the liver's Kupffer cells which rapidly digest the albumin and release the iodide label to the circulation.

Extensive studies in 40 rabbits and 100 dogs have demonstrated the feasibility, low toxicity and wide margin of safety for performing human scans with this test material. The minimum dose (15 mg/kg) of macro-aggregates, which produces only occasional transient alteration in pulmonary hemodynamics in dogs (by serial radiocardiography), is at least 150 times larger than the dose ($<$ 0.10 mg/kg) used for human scans.

Clinical trials were initiated in patients with primary and/or metastatic lung cancer. They were then extended to patients with a wide variety of lung diseases and finally to individuals with normal lungs but other serious diseases. No reactions to the test agent were encountered in the 150 patients scanned. The dose of carrier albumin did not exceed 0.2 mg/kg and the calculated radiation exposure to the lung from 100-200 μc of I^{131} is 75-150 mr and about 20 times less for I^{125}.

Pulmonary emboli and many other lesions which produce regional ischemia in the lung are detectable in the scan as areas of decreased radioactivity. On this basis the lung scan itself has diagnostic value. It also aids interpretation of chest films and pulmonary arteriograms.

W-31 *"Tc^{99m} As a Radiocolloid."* PAUL V. HARPER, KATHRINE A. LATHROP and POWELL RICHARDS (The University of Chicago, Chicago, Illinois)

The desirable physical characteristics of Tc^{99m}: 6-hour physical half-life, near absence of particle radiation, clean 140 KEV μ ray and ready available on a generator as daughter of 2.8 d Mo^{99}, stimulated a search for a method of preparing this material as a radiocolloid for scanning of liver, spleen and possibly bone marrow. An inert stable colloid of elemental sulfur has been produced by passing H_2S through 1 N HCl solution. Tc^{99m} present as pertechnetate is precipitated along with elemental sulfur possibly as the sulfide Tc_2S_7. In the presence of a protective colloid, 0.5 to 1% gelatin, the sulfur remains in colloidal form with a particle size of 50 to 150 mμ as determined by passage through millipore filters. Unreacted TcO_4^- is removed by rapid passage through IR-4B anion exchange resin washed with 1 N HCl. The solution is then diluted 1:5 with 1% gelatin for intravenous administration. 0.25 ml administered to a mouse (equivalent to 500 ml to a human) caused no apparent ill effect even though residual H_2S is present. The half-time for disappearance from the circulation is 2 to 3 minutes (dog), with 70 to 90% recoverable in the liver (mouse, dog), 5% in the spleen (mouse). Liver scans of superior resolution were obtained in patients with a variety of liver diseases. It was found necessary to block the right phrenic nerve to eliminate respiratory motion in order to take full advantage of the method. Count rates of 20,000 to 50,000 per minute were obtained with 2 millicurie quantities of isotope when using collimators of resolution usually suitable only for thyroid scanning. Estimated radiation dosage to the liver was 400 millirad/millicurie. Excretion of Tc^{99m} activity was 3% in the urine in 48 hours. Fecal excretion was barely detectable. It seems likely that it may be possible to incorporate other radionuclides in the sulfur colloid as metallic culfides.

W-32 *"Radiochemical Purity, Internal Dosimetry and Calibration of Tc^{99m}."*

E. M. SMITH (National Institutes of Health, Bethesda, Maryland)

The radiochemical purity of Tc^{99m} is being evaluated as it is eluted from the BNL generator. Also, radiochemical separations are being made, and the efficacy of these are being evaluated.

Internal dose calculations have been made for oral, intravenous and intrathecal administration of Tc^{99m} as the pertechnate ion. These calculations are based on the limited data pertaining to the distribution of Tc^{99m} as the pertechnate ion in humans and are currently being supplemented by our own studies. The following table indicates the approximate dose to various organs.

Route of Entry	*Activity of Tc^{99m}*	*Dose to Organs (mrads)*					
		Whole Body	*Gonads*		*Central Nervous System*	*Stomach*	*Upper Large Intestines*
			Male	*Female*			
Oral	10mc	48	62	128	—	—	2,545
Intravenous	1 mc	8	10	13	—	320	—
Intrathecal	1 mc	9	10	12	254	30	—

Ionization chamber and scintillation spectrometry techniques are being evaluated for the assay of Tc^{99m}. The calculated value for the gamma dose-rate constant is 0.56 r-cm²/hr-mc at 1 cm.